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NEWS 3	JAN 06	The retention policy for unread STNmail messages will change in 2009 for STN-Columbus and STN-Tokyo
NEWS 4	JAN 07	WPIDS, WPINDEX, and WPIX enhanced Japanese Patent Classification Data
NEWS 5	FEB 02	Simultaneous left and right truncation (SLART) added for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS 6	FEB 02	GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 7	FEB 06	Patent sequence location (PSL) data added to USGENE
NEWS 8	FEB 10	COMPENDEX reloaded and enhanced
NEWS 9	FEB 11	WTEXTILES reloaded and enhanced
NEWS 10	FEB 19	New patent-examiner citations in 300,000 CA/CAplus patent records provide insights into related prior art
NEWS 11	FEB 19	Increase the precision of your patent queries -- use terms from the IPC Thesaurus, Version 2009.01
NEWS 12	FEB 23	Several formats for image display and print options discontinued in USPATFULL and USPAT2
NEWS 13	FEB 23	MEDLINE now offers more precise author group fields and 2009 MeSH terms
NEWS 14	FEB 23	TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
NEWS 15	FEB 23	Three million new patent records blast AEROSPACE into STN patent clusters
NEWS 16	FEB 25	USGENE enhanced with patent family and legal status display data from INPADOCDB
NEWS 17	MAR 06	INPADOCDB and INPAFAMDB enhanced with new display formats
NEWS 18	MAR 11	EPFULL backfile enhanced with additional full-text applications and grants
NEWS 19	MAR 11	ESBIOBASE reloaded and enhanced
NEWS 20	MAR 20	CAS databases on STN enhanced with new super role for nanomaterial substances
NEWS 21	MAR 23	CA/CAplus enhanced with more than 250,000 patent equivalents from China
NEWS 22	MAR 30	IMSPATENTS reloaded and enhanced
NEWS 23	APR 03	CAS coverage of exemplified prophetic substances enhanced
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NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
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STRUCTURE FILE UPDATES:   12 APR 2009  HIGHEST RN 1133953-33-9
DICTIONARY FILE UPDATES:  12 APR 2009  HIGHEST RN 1133953-33-9

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=> e retinol
E1          917     RETINOID/BI
E2            1     RETINOIDS/BI
E3         1919 --> RETINOL/BI
E4            1     RETINOL:ALL/BI
E5          120     RETINON/BI
E6            1     RETINONA/BI
E7            1     RETINONATE/BI
E8            2     RETINONE/BI
E9          117     RETINONI/BI
E10           1     RETINONIC/BI
E11         117     RETINONITRI/BI
E12         117     RETINONITRILE/BI

=> s e3
L1         1919 RETINOL/BI
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=> e phenylbutyric
E1          282     PHENYLBUTYRATE/BI
E2            3     PHENYLBUTYRATO/BI
E3          226 --> PHENYLBUTYRIC/BI
E4            3     PHENYLBUTYRIMID/BI
E5            3     PHENYLBUTYRIMIDATE/BI
E6            1     PHENYLBUTYRIMIDIC/BI
E7            6     PHENYLBUTYRIMIDO/BI
E8            6     PHENYLBUTYRIMIDOYL/BI
E9            1     PHENYLBUTYRINE/BI
E10         110     PHENYLBUTYRO/BI
E11           1     PHENYLBUTYROAMID/BI
E12           1     PHENYLBUTYROAMIDOX/BI

=> s e3
L2          226 PHENYLBUTYRIC/BI

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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
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FILE COVERS 1907 - 13 Apr 2009  VOL 150 ISS 16
FILE LAST UPDATED: 12 Apr 2009  (20090412/ED)

Caplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

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=> s l1 and l2
         18392 L1
          6333 L2
L3           5 L1 AND L2

=> d l3 ibib abs 1-5

L3   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2008:801307  CAPLUS
DOCUMENT NUMBER:          149:135501
```

TITLE: Cosmetic compositions for smoothing and tightening of skin containing aporphine alkaloids and purine derivs.
INVENTOR(S): Heinen, Soraya; Waldmann-Laue, Marianne
PATENT ASSIGNEE(S): Henkel K.-G.a.A., Germany
SOURCE: Ger. Offen., 50pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102006062438	A1	20080703	DE 2006-102006062438	20061227
EP 1949887	A2	20080730	EP 2007-23503	20071205
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
PRIORITY APPLN. INFO.:			DE 2006-102006062438A	20061227

OTHER SOURCE(S): MARPAT 149:135501

AB The invention concerns topical applied cosmetic compns. for tightening and smoothing of skin, in particular cellulite-effected skin, which contains in a suitable cosmetic or dermatol. carrier a combination of at least one aporphine alkaloid and at least one addnl. active substance selected from purine and purine derivs., natural betaine compds., urea and alkyl or hydroxyalkyl-substituted urea, monomers, oligomers and polymers of amino acids, N-C2-C24-acylamino acids and/or esters and/or physiol. compatible salts of these substances, polysaccharides as well as mixts. of these substances. Thus a cream contained (weight/weight%): Thistle oil 3.00; Myritol 318 5.00; Novata AB 2.00; behenyl alc. 1.00; Cutina MD 2.00; cetearyl alc. 1.00; iso-Pr stearate 4.00; shea butter 2.00; Baysilone oil M 350 1.00; Controx KS 0.05; propylparaben 0.20; DowCorning 1501 fluid 1.00; Dry Flo Plus 1.00; titania 0.50; hexanediol 6.00; propylene glycol 5.00; glycerol 5.00; methylparaben 0.20; Tego Carbomer 0.40; algae extract 1.00; caomint 1.00; calmosensine 1.00; Symdiol 68 0.30; DSH-CN 5.00; Hydrovance 4.30; Kombuchka 3.00; phytokine 2.00; Ridulisse C 0.50; Liftiline 2.00; Bodyfit 3.00; perfume 0.10; water to 100.

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:441929 CAPLUS
DOCUMENT NUMBER: 148:447986
TITLE: Preparation of retinyl esters
INVENTOR(S): Boaz, Neil Warren; Clendennen, Stephanie Kay
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 10pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080085534	A1	20080410	US 2006-544152	20061006
WO 2008045185	A2	20080417	WO 2007-US20185	20070918
WO 2008045185	A3	20080612		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,				

TR, TT, TZ, UA, UG, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2006-544152 A 20061006

OTHER SOURCE(S): CASREACT 148:447986; MARPAT 148:447986

AB Long-chain esters of retinol are prepared via a chemoenzymic process from short-chain retinyl esters and an appropriate long-chain acid or ester in the presence of an enzyme. Use of various additives enhance the yield of the desired ester and facilitated its purification

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1075593 CAPLUS

DOCUMENT NUMBER: 143:352857

TITLE: Cosmetic compositions comprising an HDAC inhibitor in combination with a retinoid

INVENTOR(S): Schehlmann, Volker; Klock, Jochen; Maillan, Philippe Emmanuel; Vollhardt, Juergen H.; Rawlings, Anthony; Beumer, Raphael

PATENT ASSIGNEE(S): DSM Ip Assets B. V., Neth.

SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092283	A1	20051006	WO 2005-EP3115	20050323
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1727516	A1	20061206	EP 2005-732360	20050323
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1933802	A	20070321	CN 2005-80009488	20050323
JP 2007530487	T	20071101	JP 2007-504354	20050323
IN 2006DN05303	A	20070803	IN 2006-DN5303	20060913
KR 2007012380	A	20070125	KR 2006-719817	20060925
US 20080227868	A1	20080918	US 2006-593487	20061031

PRIORITY APPLN. INFO.: EP 2004-7281 A 20040326
WO 2005-EP3115 W 20050323

OTHER SOURCE(S): MARPAT 143:352857

AB The present invention is directed to compns. which contain a combination of at least a histone deacetylase (HDAC) inhibitor, e.g., a phenylalkylcarboxylic acid, and a retinoid. The composition is in particular a cosmetic preparation It was found that the combination of an HDAC inhibitor and retinol or a derivative thereof is in particular useful for treating wrinkles but also for thickening the epidermis and for improving hair growth. Thus, an antiaging formulation contained retinol 0.50, and phenylbutyric acid 0.30%, in addition to the conventional cosmetic

excipients.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:589747 CAPLUS
DOCUMENT NUMBER: 115:189747
ORIGINAL REFERENCE NO.: 115:32301a,32304a
TITLE: Pharmaceutical and cosmetic composition containing α-hydroxy acids, α-keto-acids, and amphoteric agents
INVENTOR(S): Yu, Ruey J.; Van Scott, Eugene J.
PATENT ASSIGNEE(S): USA
SOURCE: Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 413528	A1	19910220	EP 1990-308828	19900810
EP 413528	B1	19951115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5091171	A	19920225	US 1989-393749	19890815
US 5091171	B1	19950926		
US 5091171	B2	19970715		
CA 2019273	A1	19910215	CA 1990-2019273	19900619
CA 2019273	C	20010529		
CA 2337750	C	20021015	CA 1990-2337750	19900619
AU 9059139	A	19910221	AU 1990-59139	19900718
AU 660917	B2	19950713		
EP 671162	A2	19950913	EP 1995-105358	19900810
EP 671162	A3	19951227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 130187	T	19951215	AT 1990-308828	19900810
ES 2081936	T3	19960316	ES 1990-308828	19900810
US 5385938	B1	19920807	US 1992-925877	19920807
US 5385938	A	19950131		
US 5702688	A	19971230	US 1993-135841	19931007
US 5637615	A	19970610	US 1995-467153	19950606
US 5643961	A	19970701	US 1995-466737	19950606
US 5643962	A	19970701	US 1995-466740	19950606
US 5643952	A	19970701	US 1995-466770	19950606
US 5643953	A	19970701	US 1995-467156	19950606
US 5643963	A	19970701	US 1995-471523	19950606
US 5648395	A	19970715	US 1995-466739	19950606
US 5648391	A	19970715	US 1995-469812	19950606
US 5648388	A	19970715	US 1995-471511	19950606
US 5650436	A	19970722	US 1995-467134	19950606
US 5650437	A	19970722	US 1995-470060	19950606
US 5650440	A	19970722	US 1995-471513	19950606
US 5652267	A	19970729	US 1995-469814	19950606
US 5654340	A	19970805	US 1995-467989	19950606
US 5656665	A	19970812	US 1995-466771	19950606
US 5656666	A	19970812	US 1995-470829	19950606
US 5670542	A	19970923	US 1995-465700	19950606
US 5670543	A	19970923	US 1995-471521	19950606
US 5674899	A	19971007	US 1995-465704	19950606
US 5674903	A	19971007	US 1995-468079	19950606
US 5677339	A	19971014	US 1995-466820	19950606

US 5677340	A	19971014	US 1995-468077	19950606
US 5716992	A	19980210	US 1995-469811	19950606
US 5827882	A	19981027	US 1995-465695	19950606
US 5654336	A	19970805	US 1995-483328	19950607
US 5681853	A	19971028	US 1995-472317	19950607
US 5684044	A	19971104	US 1995-472315	19950607
US 5690967	A	19971125	US 1995-472310	19950607
AU 9533110	A	19960215	AU 1995-33110	19951006
AU 701962	B2	19990211		
US 6060512	A	20000509	US 1998-185608	19981104
US 6051609	A	20000418	US 1998-222997	19981230
US 6191167	B1	20010220	US 1999-255702	19990223
US 20030083380	A1	20030501	US 2000-729981	20001206
US 6767924	B2	20040727		

PRIORITY APPLN. INFO.:	US 1989-393749	A	19890815
	US 1986-945680	B2	19861223
	US 1990-469738	B1	19900119
	CA 1990-2019273	A3	19900619
	EP 1990-308828	A3	19900810
	US 1992-840149	B1	19920224
	US 1993-135841	A1	19931007
	US 1997-926030	A1	19970909
	US 1997-998864	A1	19971229
	US 1997-998871	A3	19971229
	US 1998-185608	A1	19981104
	US 2000-513225	B1	20000225

OTHER SOURCE(S): MARPAT 115:189747

AB A pharmaceutical or cosmetic topical composition comprises an amphoteric or pseudoamphoteric agent and an α-hydroxy acid, an α-keto acid or a related compound for the treatment of skin disorders. A composition for dandruff or dry skin contained glycolic acid 7.6, L-arginine 8.7g, water 60, propylene glycol 20, and EtOH up to 100 mL. The pH of the composition was 3.0.

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	1959:78685 CAPLUS
DOCUMENT NUMBER:	53:78685
ORIGINAL REFERENCE NO.:	53:14289i,14290a-b
TITLE:	Comparative chemical and clinical studies on the blood of treated and untreated patients with arteriosclerosis
AUTHOR(S):	Voigt, K. D.; Gadermann, E.; Klempien, E. J.; Sartori, C.
CORPORATE SOURCE:	Univ. Hamburg-Eppendorf, Germany
SOURCE:	Deutsches Archiv fuer Klinische Medizin (1957), 204, 409-29 CODEN: DAKMAJ; ISSN: 0366-8576
DOCUMENT TYPE:	Journal
LANGUAGE:	Unavailable

AB In 77 of 147 subjects with manifest arteriosclerosis there were significant changes in blood lipides and proteins. In 17 the cholesterol content was within normal limits, and in 37 the lipide-protein picture was normal but other pathol. conditions were present. Treatment with Na or Mg salt of α-phenylethylacetic acid, or with Rovigon or Liquemin influenced markedly the content of serum lipides and proteins as long as the treatment continued, and there was frequently some clinical or subjective improvement. No correlation was found between function and the morphological or blood chemical changes.

=> file caplus medline

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)       SINCE FILE      TOTAL
                                                        ENTRY    SESSION
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=> s 4-phenylbutyr? and retinol
L4            1 4-PHENYLBUTYR? AND RETINOL

=> d l4 ibib abs

L4   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2008:441929  CAPLUS
DOCUMENT NUMBER:          148:447986
TITLE:                    Preparation of retinyl esters
INVENTOR(S):              Boaz, Neil Warren; Clendennen, Stephanie Kay
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 10pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 20080085534        A1    20080410    US 2006-544152          20061006
     WO 2008045185         A2    20080417    WO 2007-US20185         20070918
     WO 2008045185         A3    20080612
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
             MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
             PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRIORITY APPLN. INFO.:                       US 2006-544152      A  20061006
OTHER SOURCE(S):          CASREACT 148:447986; MARPAT 148:447986
AB   Long-chain esters of retinol are prepared via a chemoenzymic
     process from short-chain retinyl esters and an appropriate long-chain acid
     or ester in the presence of an enzyme.  Use of various additives enhance
     the yield of the desired ester and facilitated its purification


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 NEWS  5  FEB 02  Simultaneous left and right truncation (SLART) added
                  for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
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                  patent records provide insights into related prior
                  art
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 NEWS 13  FEB 23  MEDLINE now offers more precise author group fields
                  and 2009 MeSH terms
 NEWS 14  FEB 23  TOXCENTER updates mirror those of MEDLINE - more
                  precise author group fields and 2009 MeSH terms
 NEWS 15  FEB 23  Three million new patent records blast AEROSPACE into
                  STN patent clusters
 NEWS 16  FEB 25  USGENE enhanced with patent family and legal status
                  display data from INPADOCDB
 NEWS 17  MAR 06  INPADOCDB and INPAFAMDB enhanced with new display
                  formats
 NEWS 18  MAR 11  EPFULL backfile enhanced with additional full-text
                  applications and grants
 NEWS 19  MAR 11  ESBIOBASE reloaded and enhanced
 NEWS 20  MAR 20  CAS databases on STN enhanced with new super role
                  for nanomaterial substances
 NEWS 21  MAR 23  CA/CAplus enhanced with more than 250,000 patent
                  equivalents from China
 NEWS 22  MAR 30  IMSPATENTS reloaded and enhanced
 NEWS 23  APR 03  CAS coverage of exemplified prophetic substances
                  enhanced
 NEWS 24  APR 07  STN is raising the limits on saved answers

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
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SESSION RESUMED IN FILE 'HOME' AT 11:37:17 ON 14 APR 2009
FILE 'HOME' ENTERED AT 11:37:17 ON 14 APR 2009

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.44	0.44

FILE 'CAPLUS' ENTERED AT 11:37:49 ON 14 APR 2009
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FILE COVERS 1907 - 14 Apr 2009 VOL 150 ISS 16
FILE LAST UPDATED: 13 Apr 2009 (20090413/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> file caplus medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.50       0.94

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FILE 'MEDLINE' ENTERED AT 11:37:52 ON 14 APR 2009

=> s histone deacetylase and retin?
L1        1329 HISTONE DEACETYLASE AND RETIN?

=> s l1 and cosmetic?
L2           4 L1 AND COSMETIC?

=> d l2 ibib abs 1-4

L2   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2006:1202261  CAPLUS
DOCUMENT NUMBER:          145:495768
TITLE:                    Soft tissue implants, anti-scarring agents, and
                          therapeutic compositions
INVENTOR(S):              Hunter, William L.; Toleikis, Philip M.; Gravett,
                          David M.; Maiti, Arpita; Liggins, Richard T.;
                          Takacs-Cox, Aniko; Avelar, Rui; Signore, Pierre E.;
                          Loss, Troy A. E.; Hutchinson, Anne; McDonald-Jones,
                          Gaye; Lakhani, Fara
PATENT ASSIGNEE(S):       Angiotech International A.-G., Switz.
SOURCE:                   PCT Int. Appl., 2979pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2006121521         A2    20061116    WO 2006-US11690          20060331
     WO 2006121521         A3    20070111
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     WO 2006121522         A2    20061116    WO 2006-US11726          20060331
     WO 2006121522         A3    20080502
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
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SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW
RW: AP, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
EA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, EP, AT, BE, BG, CH, CY,
CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV,
MC, NL, PL, PT, RO, SE, SI, SK, TR, OA, BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2005-679293P P 20050510
US 2005-679962P P 20050510
US 2005-679291P P 20050510

AB Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and nasal implants) are used in combination with an anti-scarring agent in order to inhibit scarring that may otherwise occur when the implant is placed within an animal.

L2 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:513522 CAPLUS
DOCUMENT NUMBER: 145:21119
TITLE: Harnessing network biology to improve drug discovery
INVENTOR(S): MacDonald, Marnie L.; Westwick, John K.; Keon, Brigitte; Lamerdin, Jane; Michnick, Stephen W.
PATENT ASSIGNEE(S): Odyssey Thera, Inc., USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006058014	A2	20060601	WO 2005-US42344	20051122
WO 2006058014	A3	20070426		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 20060160109	A1	20060720	US 2005-282745	20051121
AU 2005309649	A1	20060601	AU 2005-309649	20051122
CA 2590331	A1	20060601	CA 2005-2590331	20051122
EP 1836631	A2	20070926	EP 2005-824951	20051122
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: US 2004-629558P P 20041122
US 2005-282745 A 20051121
WO 2005-US42344 W 20051122

AB This invention provides principles, methods and compns. for ascertaining the mechanism of action of pharmacol. important compds. in the context of network biol., across the entire scope of the complex pathways of living cells. Importantly, the principles, methods and compns. provided allow a rapid assessment of the on-pathway and off-pathway effects of lead compds. and drug candidates in living cells, and comparisons of lead compds. with well-characterized drugs and toxicants to identify patterns associated with

efficacy and toxicity. The invention will be useful in improving the drug discovery process, in particular by identifying drug leads with desired safety and efficacy and in effecting early attrition of compds. with potential adverse effects in man.

L2 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1075593 CAPLUS
DOCUMENT NUMBER: 143:352857
TITLE: Cosmetic compositions comprising an HDAC inhibitor in combination with a retinoid
INVENTOR(S): Schehlmann, Volker; Klock, Jochen; Maillan, Philippe Emmanuel; Vollhardt, Juergen H.; Rawlings, Anthony; Beumer, Raphael
PATENT ASSIGNEE(S): DSM Ip Assets B. V., Neth.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092283	A1	20051006	WO 2005-EP3115	20050323
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1727516	A1	20061206	EP 2005-732360	20050323
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1933802	A	20070321	CN 2005-80009488	20050323
JP 2007530487	T	20071101	JP 2007-504354	20050323
IN 2006DN05303	A	20070803	IN 2006-DN5303	20060913
KR 2007012380	A	20070125	KR 2006-719817	20060925
US 20080227868	A1	20080918	US 2006-593487	20061031
PRIORITY APPLN. INFO.:			EP 2004-7281 A	20040326
			WO 2005-EP3115 W	20050323

OTHER SOURCE(S): MARPAT 143:352857
AB The present invention is directed to compns. which contain a combination of at least a histone deacetylase (HDAC) inhibitor, e.g., a phenylalkylcarboxylic acid, and a retinoid. The composition is in particular a cosmetic preparation It was found that the combination of an HDAC inhibitor and retinol or a derivative thereof is in particular useful for treating wrinkles but also for thickening the epidermis and for improving hair growth. Thus, an antiaging formulation contained retinol 0.50, and phenylbutyric acid 0.30%, in addition to the conventional cosmetic excipients.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:155393 CAPLUS
DOCUMENT NUMBER: 142:225268
TITLE: Composition for treatment of degradation of collagen

fibers induced by exposure to sun light
INVENTOR(S): Fagot, Dominique; Bernerd, Francoise
PATENT ASSIGNEE(S): L'oreal, Fr.
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1508328	A1	20050223	EP 2004-291941	20040729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
FR 2858932	A1	20050225	FR 2003-10103	20030822
CA 2478783	A1	20050222	CA 2004-2478783	20040811
US 20050058611	A1	20050317	US 2004-922929	20040823
JP 2005132823	A	20050526	JP 2004-242323	20040823

PRIORITY APPLN. INFO.: FR 2003-10103 A 20030822
US 2003-530233P P 20031218

AB A cosmetic composition for prevention or treatment of degradation of collagen fibers induced by exposure to sun light, particularly UVA/UVB, comprises an inhibitor of production of photoinduced cytosol. keratinocyte factor. The inhibitor is sodium butyrate (I). A cream contained I 1, 10% lycopene 0.001, glycerol stearate 2, Polysorbate-60 1, stearic acid 1.4, triethanolamine 0.7, Carbomer 0.4, karite butter liquid fraction 12, perhydrosqualene 12, antioxidants q.s., perfume q.s., preservatives q.s. and water q.s. 100%.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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NEWS 4	JAN 07	WPIDS, WPINDEX, and WPIX enhanced Japanese Patent Classification Data
NEWS 5	FEB 02	Simultaneous left and right truncation (SLART) added for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS 6	FEB 02	GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 7	FEB 06	Patent sequence location (PSL) data added to USGENE
NEWS 8	FEB 10	COMPENDEX reloaded and enhanced
NEWS 9	FEB 11	WTEXTILES reloaded and enhanced
NEWS 10	FEB 19	New patent-examiner citations in 300,000 CA/CAplus

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                  patent records provide insights into related prior
                  art
 NEWS 11  FEB 19  Increase the precision of your patent queries -- use
                  terms from the IPC Thesaurus, Version 2009.01
 NEWS 12  FEB 23  Several formats for image display and print options
                  discontinued in USPATFULL and USPAT2
 NEWS 13  FEB 23  MEDLINE now offers more precise author group fields
                  and 2009 MeSH terms
 NEWS 14  FEB 23  TOXCENTER updates mirror those of MEDLINE - more
                  precise author group fields and 2009 MeSH terms
 NEWS 15  FEB 23  Three million new patent records blast AEROSPACE into
                  STN patent clusters
 NEWS 16  FEB 25  USGENE enhanced with patent family and legal status
                  display data from INPADOCDB
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                  formats
 NEWS 18  MAR 11  EPFULL backfile enhanced with additional full-text
                  applications and grants
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 NEWS 20  MAR 20  CAS databases on STN enhanced with new super role
                  for nanomaterial substances
 NEWS 21  MAR 23  CA/CAplus enhanced with more than 250,000 patent
                  equivalents from China
 NEWS 22  MAR 30  IMSPATENTS reloaded and enhanced
 NEWS 23  APR 03  CAS coverage of exemplified prophetic substances
                  enhanced
 NEWS 24  APR 07  STN is raising the limits on saved answers

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              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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=> s histone deacetylase and wrinkle?
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commands which can be used in this file.

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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.22       0.22

FILE 'CAPLUS' ENTERED AT 11:55:22 ON 14 APR 2009
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FILE 'MEDLINE' ENTERED AT 11:55:22 ON 14 APR 2009

=> s histone deacetylase and wrinkle?
L1 6 HISTONE DEACETYLASE AND WRINKLE?

=> d l1 ibib abs 1-6

L1 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:823515 CAPLUS
DOCUMENT NUMBER: 145:255514
TITLE: Histone deacetylase inhibitor which containing n-butyric acid which has excellent preventing or improving effects on skin wrinkle and composition containing the same
INVENTOR(S): Bang, Sun Lie; Lee, Jae Yong
PATENT ASSIGNEE(S): C. F. Co., Ltd., S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2005018826	A	20050228	KR 2005-2836	20050112

PRIORITY APPLN. INFO.: KR 2005-2836 20050112

AB Provided is a histone deacetylase inhibitor containing n-butyric acid which has excellent preventing or improving effects on the skin wrinkle by enhancing the expression of proteins as main structural components of the dermis while inhibiting the expression of proteases. Also, a composition containing the same is provided which is useful for medicines and cosmetics. The histone deacetylase inhibitor containing n-butyric acid prevents and improves the skin wrinkle by enhancing the expression of proteins including collagen and elastin which are main structural components of the dermis, while inhibiting the expression of proteases. The composition of a cosmetic or a medicine is characterized by containing the histone deacetylase inhibitor.

L1 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1075593 CAPLUS
DOCUMENT NUMBER: 143:352857
TITLE: Cosmetic compositions comprising an HDAC inhibitor in combination with a retinoid
INVENTOR(S): Schehlmann, Volker; Klock, Jochen; Maillan, Philippe Emmanuel; Vollhardt, Juergen H.; Rawlings, Anthony; Beumer, Raphael
PATENT ASSIGNEE(S): DSM Ip Assets B. V., Neth.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005092283	A1	20051006	WO 2005-EP3115	20050323
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1727516	A1	20061206	EP 2005-732360	20050323
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1933802	A	20070321	CN 2005-80009488	20050323
JP 2007530487	T	20071101	JP 2007-504354	20050323
IN 2006DN05303	A	20070803	IN 2006-DN5303	20060913
KR 2007012380	A	20070125	KR 2006-719817	20060925
US 20080227868	A1	20080918	US 2006-593487	20061031
PRIORITY APPLN. INFO.:			EP 2004-7281 A	20040326
			WO 2005-EP3115 W	20050323

OTHER SOURCE(S): MARPAT 143:352857

AB The present invention is directed to compns. which contain a combination of at least a histone deacetylase (HDAC) inhibitor, e.g., a phenylalkylcarboxylic acid, and a retinoid. The composition is in particular a cosmetic preparation It was found that the combination of an HDAC inhibitor and retinol or a derivative thereof is in particular useful for treating wrinkles but also for thickening the epidermis and for improving hair growth. Thus, an antiaging formulation contained retinol 0.50, and phenylbutyric acid 0.30%, in addition to the conventional cosmetic excipients.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:381458 CAPLUS
DOCUMENT NUMBER: 133:12738
TITLE: Retinoyloxy aryl-substituted alkylene butyrates useful for the treatment of cancer and other proliferative diseases
INVENTOR(S): Nudelman, Abraham; Rephaeli, Ada
PATENT ASSIGNEE(S): Bar-Ilan University, Israel; Mor Research Applications
SOURCE: U.S., 9 pp., Cont.-in-part of U.S. 5,710,176.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6071923	A	20000606	US 1997-883219	19970626
US 5710176	A	19980120	US 1994-306422	19940916
CA 2258593	A1	19980108	CA 1997-2258593	19970701
JP 2002514161	T	20020514	JP 1998-504403	19970701
PRIORITY APPLN. INFO.:			US 1994-306422 A2	19940916
			US 1996-674481 A	19960702
			US 1997-883219 A	19970626
			WO 1997-US11452 W	19970701

OTHER SOURCE(S): MARPAT 133:12738

AB Retinoyloxy(aryl-substituted)-alkylene butyrate compds. are provided, as are pharmaceutical compns. containing them and methods of treating, preventing, or ameliorating cancer and other proliferative diseases comprising administering a compound of the invention or a pharmaceutically acceptable salt or prodrug thereof. The compds. of the invention are also useful in methods of inhibiting histone deacetylase, ameliorating wrinkles, treating or ameliorating dermatol. disorders, inducing wound healing, treating cutaneous ulcers and treating gastrointestinal disorders.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1998:55520 CAPLUS
DOCUMENT NUMBER: 128:119667
ORIGINAL REFERENCE NO.: 128:23363a,23366a
TITLE: Retinoyloxy(substituted)alkylene butyrates useful for the treatment of cancer and other proliferative diseases
INVENTOR(S): Rephaeli, Ada; Nudelman, Abraham
PATENT ASSIGNEE(S): Bar-Ilan University, Israel; Kupat Holim Health Insurance Institution of the General Federation of Labor; Rephaeli, Ada
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9800127	A1	19980108	WO 1997-US11452		19970701
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
US 6040342	A	20000321	US 1996-674481		19960702
AU 9735880	A	19980121	AU 1997-35880		19970701
EP 927033	A1	19990707	EP 1997-932417		19970701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002514161	T	20020514	JP 1998-504403		19970701
PRIORITY APPLN. INFO.:			US 1996-674481	A	19960702
			US 1994-306422	A2	19940916
			US 1997-883219	A	19970626
			WO 1997-US11452	W	19970701

OTHER SOURCE(S): MARPAT 128:119667

AB This invention relates to novel retinoyloxy(substituted)alkylene butyrate compds. and pharmaceutical compns. containing same, to methods of treating, preventing or ameliorating cancer and other proliferative diseases in a subject in need of such treatment by comprising administering those compds., pharmaceutically-acceptable salts or prodrugs thereof to a patient. The compds. of the invention are also useful in methods of inhibiting histone deacetylase, ameliorating wrinkles, treating or ameliorating dermatol. disorders, inducing wound healing, treating cutaneous ulcers and treating gastrointestinal disorders. 13-Trans-retinoyloxymethyl butyrate was prepared and showed

greated activity on the level of cell differentiation than either retinoic acid or butyric acid alone or a combination of the two.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 5 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2008293514 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18454196
TITLE: Drosophila histone deacetylase-3 controls imaginal disc size through suppression of apoptosis.
AUTHOR: Zhu Changqi C; Bornemann Douglas J; Zhitomirsky David; Miller Ellen L; O'Connor Michael B; Simon Jeffrey A
CORPORATE SOURCE: Department of Genetics, Cell Biology and Development, University of Minnesota, Minneapolis, Minnesota, United States of America.
CONTRACT NUMBER: GM49850 (United States NIGMS NIH HHS)
(United States Howard Hughes Medical Institute)
SOURCE: PLoS genetics, (2008 Feb) Vol. 4, No. 2, pp. e1000009. Electronic Publication: 2008-02-29.
Journal code: 101239074. E-ISSN: 1553-7404.
Report No.: NLM-PMC2265479.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200806
ENTRY DATE: Entered STN: 6 May 2008
Last Updated on STN: 14 Jun 2008
Entered Medline: 13 Jun 2008

AB Histone deacetylases (HDACs) execute biological regulation through post-translational modification of chromatin and other cellular substrates. In humans, there are eleven HDACs, organized into three distinct subfamilies. This large number of HDACs raises questions about functional overlap and division of labor among paralogs. In vivo roles are simpler to address in Drosophila, where there are only five HDAC family members and only two are implicated in transcriptional control. Of these two, HDAC1 has been characterized genetically, but its most closely related paralog, HDAC3, has not. Here we describe the isolation and phenotypic characterization of hdac3 mutations. We find that both hdac3 and hdac1 mutations are dominant suppressors of position effect variegation, suggesting functional overlap in heterochromatin regulation. However, all five hdac3 loss-of-function alleles are recessive lethal during larval/pupal stages, indicating that HDAC3 is essential on its own for Drosophila development. The mutant larvae display small imaginal discs, which result from abnormally elevated levels of apoptosis. This cell death occurs as a cell-autonomous response to HDAC3 loss and is accompanied by increased expression of the pro-apoptotic gene, hid. In contrast, although HDAC1 mutants also display small imaginal discs, this appears to result from reduced proliferation rather than from elevated apoptosis. The connection between HDAC loss and apoptosis is important since HDAC inhibitors show anticancer activities in animal models through mechanisms involving apoptotic induction. However, the specific HDACs implicated in tumor cell killing have not been identified. Our results indicate that protein deacetylation by HDAC3 plays a key role in suppression of apoptosis in Drosophila imaginal tissue.

L1 ANSWER 6 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2008250327 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18410726

TITLE: Epigenetic blocking of an enhancer region controls irradiation-induced proapoptotic gene expression in Drosophila embryos.
AUTHOR: Zhang Yanping; Lin Nianwei; Carroll Pamela M; Chan Gina; Guan Bo; Xiao Hong; Yao Bing; Wu Samuel S; Zhou Lei
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, College of Medicine, University of Florida, Gainesville, FL 32610, USA.
CONTRACT NUMBER: CA95542 (United States NCI NIH HHS)
R01 CA095542-03 (United States NCI NIH HHS)
R01 CA095542-04 (United States NCI NIH HHS)
R01 CA095542-05 (United States NCI NIH HHS)
SOURCE: Developmental cell, (2008 Apr) Vol. 14, No. 4, pp. 481-93.
Journal code: 101120028. ISSN: 1534-5807.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GEO-GSE1005; GEO-GSM15877; GEO-GSM15878; GEO-GSM15879; GEO-GSM15880; GEO-GSM15881; GEO-GSM15882; GEO-GSM15883; GEO-GSM15884; GEO-GSM15885; GEO-GSM15886; GEO-GSM15887; GEO-GSM15888
ENTRY MONTH: 200805
ENTRY DATE: Entered STN: 16 Apr 2008
Last Updated on STN: 20 May 2008
Entered Medline: 19 May 2008

AB Drosophila embryos are highly sensitive to gamma-ray-induced apoptosis at early but not later, more differentiated stages during development. Two proapoptotic genes, reaper and hid, are upregulated rapidly following irradiation. However, in post-stage-12 embryos, in which most cells have begun differentiation, neither proapoptotic gene can be induced by high doses of irradiation. Our study indicates that the sensitive-to-resistant transition is due to epigenetic blocking of the irradiation-responsive enhancer region (IRER), which is located upstream of reaper but is also required for the induction of hid in response to irradiation. This IRER, but not the transcribed regions of reaper/hid, becomes enriched for trimethylated H3K27/H3K9 and forms a heterochromatin-like structure during the sensitive-to-resistant transition. The functions of histone-modifying enzymes Hdac1(rpd3) and Su(var)3-9 and PcG proteins Su(z)12 and Polycomb are required for this process. Thus, direct epigenetic regulation of two proapoptotic genes controls cellular sensitivity to cytotoxic stimuli.

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 NEWS  3  FEB 02  Simultaneous left and right truncation (SLART) added
                  for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
 NEWS  4  FEB 02  GENBANK enhanced with SET PLURALS and SET SPELLING
 NEWS  5  FEB 06  Patent sequence location (PSL) data added to USGENE
 NEWS  6  FEB 10  COMPENDEX reloaded and enhanced
 NEWS  7  FEB 11  WTEXTILES reloaded and enhanced
 NEWS  8  FEB 19  New patent-examiner citations in 300,000 CA/CAplus
                  patent records provide insights into related prior
                  art
 NEWS  9  FEB 19  Increase the precision of your patent queries -- use
                  terms from the IPC Thesaurus, Version 2009.01
 NEWS 10  FEB 23  Several formats for image display and print options
                  discontinued in USPATFULL and USPAT2
 NEWS 11  FEB 23  MEDLINE now offers more precise author group fields
                  and 2009 MeSH terms
 NEWS 12  FEB 23  TOXCENTER updates mirror those of MEDLINE - more
                  precise author group fields and 2009 MeSH terms
 NEWS 13  FEB 23  Three million new patent records blast AEROSPACE into
                  STN patent clusters
 NEWS 14  FEB 25  USGENE enhanced with patent family and legal status
                  display data from INPADOCDB
 NEWS 15  MAR 06  INPADOCDB and INPAFAMDB enhanced with new display
                  formats
 NEWS 16  MAR 11  EPFULL backfile enhanced with additional full-text
                  applications and grants
 NEWS 17  MAR 11  ESBIOBASE reloaded and enhanced
 NEWS 18  MAR 20  CAS databases on STN enhanced with new super role
                  for nanomaterial substances
 NEWS 19  MAR 23  CA/CAplus enhanced with more than 250,000 patent
                  equivalents from China
 NEWS 20  MAR 30  IMSPATENTS reloaded and enhanced
 NEWS 21  APR 03  CAS coverage of exemplified prophetic substances
                  enhanced
 NEWS 22  APR 07  STN is raising the limits on saved answers
 NEWS 23  APR 24  CA/CAplus now has more comprehensive patent assignee
                  information
 NEWS 24  APR 26  USPATFULL and USPAT2 enhanced with patent
                  assignment/reassignment information
 NEWS 25  APR 28  CAS patent authority coverage expanded
 NEWS 26  APR 28  ENCOMPLIT/ENCOMPLIT2 search fields enhanced
 NEWS 27  APR 28  Limits doubled for structure searching in CAS
                  REGISTRY

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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=> file caplus medline biosis embase
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                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.22       0.22

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=> s retinol and ?phenylbutyric
L1            5 RETINOL AND ?PHENYLBUTYRIC

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2            5 DUP REM L1 (0 DUPLICATES REMOVED)

=> d l2 ibib abs 1-5

L2   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2008:441929  CAPLUS
DOCUMENT NUMBER:          148:447986
TITLE:                    Preparation of retinyl esters
INVENTOR(S):              Boaz, Neil Warren; Clendennen, Stephanie Kay
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 10pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 20080085534        A1    20080410    US 2006-544152          20061006
     WO 2008045185         A2    20080417    WO 2007-US20185         20070918
     WO 2008045185         A3    20080612
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
             MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
             PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRIORITY APPLN. INFO.:                       US 2006-544152      A  20061006
OTHER SOURCE(S):          CASREACT 148:447986; MARPAT 148:447986
AB   Long-chain esters of retinol are prepared via a chemoenzymic
     process from short-chain retinyl esters and an appropriate long-chain acid
```

or ester in the presence of an enzyme. Use of various additives enhance the yield of the desired ester and facilitated its purification

L2 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1075593 CAPLUS
DOCUMENT NUMBER: 143:352857
TITLE: Cosmetic compositions comprising an HDAC inhibitor in combination with a retinoid
INVENTOR(S): Schehlmann, Volker; Klock, Jochen; Maillan, Philippe Emmanuel; Vollhardt, Juergen H.; Rawlings, Anthony; Beumer, Raphael
PATENT ASSIGNEE(S): Dsm Ip Assets B.V., Neth.; Schehlmann, Volker; Klock, Jochen; Maillan, Philippe Emmanuel; Vollhardt, Juergen H.; Rawlings, Anthony; Beumer, Raphael
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092283	A1	20051006	WO 2005-EP3115	20050323
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1727516	A1	20061206	EP 2005-732360	20050323
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1933802	A	20070321	CN 2005-80009488	20050323
JP 2007530487	T	20071101	JP 2007-504354	20050323
IN 2006DN05303	A	20070803	IN 2006-DN5303	20060913
KR 2007012380	A	20070125	KR 2006-719817	20060925
US 20080227868	A1	20080918	US 2006-593487	20061031
PRIORITY APPLN. INFO.:			EP 2004-7281 A	20040326
			WO 2005-EP3115 W	20050323

OTHER SOURCE(S): MARPAT 143:352857
AB The present invention is directed to compns. which contain a combination of at least a histone deacetylase (HDAC) inhibitor, e.g., a phenylalkylcarboxylic acid, and a retinoid. The composition is in particular a cosmetic preparation It was found that the combination of an HDAC inhibitor and retinol or a derivative thereof is in particular useful for treating wrinkles but also for thickening the epidermis and for improving hair growth. Thus, an antiaging formulation contained retinol 0.50, and phenylbutyric acid 0.30%, in addition to the conventional cosmetic excipients.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 5 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004449704 EMBASE
TITLE: α(1)-antitrypsin deficiency.ovrhdot.6: New and

emerging treatments for α(1)-antitrypsin deficiency.
AUTHOR: Sandhaus, R.A., Dr. (correspondence)
CORPORATE SOURCE: Alpha-1 Program, Natl. Jewish Med. and Res. Center, Southside Building G106, 1400 Jackson Street, Denver, CO 80206, United States. rasandhaus@alphaone.org
SOURCE: Thorax, (Oct 2004) Vol. 59, No. 10, pp. 904-909.
Refs: 102
ISSN: 0040-6376 CODEN: THORA7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Nov 2004
Last Updated on STN: 19 Nov 2004
AB Alpha-1-antitrypsin (AAT) deficiency is a genetic condition that increases the risk of developing lung and liver disease, as well as other associated conditions. Most treatment of affected individuals is not specifically directed at AAT deficiency but focuses on the resultant disease state. The only currently available specific therapeutic agent-namely, intravenous augmentation with plasma derived AAT protein - is marketed in a limited number of countries. Treatments aimed at correcting the underlying genetic abnormality, supplementing or modifying the gene product, and halting or reversing organ injury are now beginning to emerge. These innovative approaches may prove effective at modifying or eliminating diseases association with AAT deficiency.

L2 ANSWER 4 OF 5 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003442653 EMBASE
TITLE: Overview.
AUTHOR: VanItallie, Theodore B., Dr. (correspondence)
CORPORATE SOURCE: Div. of Endocrinol., Diabetes/Nutr., Medical Science, St. Luke's-Roosevelt Hospital Center, New York, NY, United States.
AUTHOR: VanItallie, Theodore B., Dr. (correspondence)
CORPORATE SOURCE: Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, NY, United States.
AUTHOR: VanItallie, Theodore B., Dr. (correspondence)
CORPORATE SOURCE: PO Box 775, Boca Grande, FL 33921, United States.
SOURCE: Metabolism: Clinical and Experimental, (Oct 2003) Vol. 52, No. SUPPL. 2, pp. 2-3.
ISSN: 0026-0495 CODEN: METAAJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
020 Gerontology and Geriatrics
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2003
Last Updated on STN: 13 Nov 2003

L2 ANSWER 5 OF 5 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003047678 EMBASE
TITLE: Retinoic acid metabolism and mechanism of action: A review.
AUTHOR: Marill, Julie; Idres, Nadia; Capron, Claude C.; Nguyen,

Eric; Chabot, Guy G.
CORPORATE SOURCE: INSERM UMR-496, Institut Univ. d'Hematologie, Hopital Saint-Louis, 1 avenue Claude-Vellefaux, 75475 Paris 10, France. gchabot@chu-stlouis.fr
AUTHOR: Chabot, G.G. (correspondence)
CORPORATE SOURCE: Institut Univ. d'Hematologie, Hopital Saint-Louis, INSERM U-496, 1 avenue Claude-Vellefaux, 75475 Paris 10, France. gchabot@chu-stlouis.fr
SOURCE: Current Drug Metabolism, (Feb 2003) Vol. 4, No. 1, pp. 1-10.
Refs: 97
ISSN: 1389-2002 CODEN: CDMUBU
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
025 Hematology
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Feb 2003
Last Updated on STN: 7 Feb 2003
AB Retinoids are vitamin A (retinol) derivatives essential for normal embryo development and epithelial differentiation. These compounds are also involved in chemoprevention and differentiation therapy of some cancers, with particularly impressive results in the management of acute promyelocytic leukemia (APL). Although highly effective in APL therapy, resistance to retinoic acid (RA) develops rapidly. The causes of this resistance are not completely understood and the following factors have been involved: increased metabolism, increased expression of RA binding proteins, P-glycoprotein expression, and mutations in the ligand binding domain of RARα. RA exerts its molecular actions mainly through RAR and RXR nuclear receptors. In addition to the nuclear receptor based mechanism of RA action, covalent binding of RA to cell macromolecules has been reported. RA derives from retinol by oxidation through retinol and retinal dehydrogenases, and several cytochrome P450s (CYPs). RA is thereafter oxidized to several metabolites by a panel of CYPs that differs for the different RA isomers. Phase II metabolism, mainly glucuronidation, is also observed. The role RA metabolism plays in the expression of its biological actions is not completely understood: in several systems, metabolism decreases RA activity, whereas in other systems metabolism appears involved in its action. In addition, several RA metabolites have shown activity and cannot be classified as only catabolites. Therapy of cancer with retinoids is still in its infancy, but the use of new analogues with improved pharmacological properties, along with combination with other drugs, could undoubtedly improve the management of several cancers in the future.

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 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  AUG 10  Time limit for inactive STN sessions doubles to 40
                  minutes
 NEWS  3  AUG 18  COMPENDEX indexing changed for the Corporate Source
                  (CS) field
 NEWS  4  AUG 24  ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
 NEWS  5  AUG 24  CA/CAplus enhanced with legal status information for
                  U.S. patents
 NEWS  6  SEP 09  50 Millionth Unique Chemical Substance Recorded in
                  CAS REGISTRY
 NEWS  7  SEP 11  WPIDS, WPINDEX, and WPIX now include Japanese FTERM
                  thesaurus
 NEWS  8  OCT 21  Derwent World Patents Index Coverage of Indian and
                  Taiwanese Content Expanded
 NEWS  9  OCT 21  Derwent World Patents Index enhanced with human
                  translated claims for Chinese Applications and
                  Utility Models
 NEWS 10  OCT 27  Free display of legal status information in CA/CAplus,
                  USPATFULL, and USPAT2 in the month of November.

 NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
              AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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=> s retino? and (histone (s) deacetylase) and (skin or topical or epiderm? or
keratin?)
L1          275 RETINO? AND (HISTONE (S) DEACETYLASE) AND (SKIN OR TOPICAL OR
                EPIDERM? OR KERATIN?)

=> s l1 and synerg?
L2           20 L1 AND SYNERG?

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           20 DUP REM L2 (0 DUPLICATES REMOVED)

=> d l3 ibib abs 1-20

L3   ANSWER 1 OF 20  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2009:739059  CAPLUS
DOCUMENT NUMBER:          151:86657
TITLE:                    Combinations of therapeutic agents comprising vascular
                          disrupting agent such as
                          5,6-dimethylxanthenone-4-acetic acid, for treating
                          cancer
INVENTOR(S):              Evans, Dean Brent; Jacques, Christian J.
PATENT ASSIGNEE(S):       Novartis A.-G., Switz.
SOURCE:                   PCT Int. Appl., 57pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2009076170         A2    20090618    WO 2008-US85535         20081204
     WO 2009076170         A3    20090730
         W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
             CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,
             FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
             KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
             ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
```

PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2007-13335P P 20071213

AB The invention relates to a combination comprising vascular disrupting agent (VDA), such as 5,6-dimethylxanthenone-4-acetic acid or a pharmaceutically acceptable salt, ester or prodrug thereof; and one or more pharmaceutically active agents; pharmaceutical compns. comprising said combination; methods of treatment comprising said combination; processes for making said combination; and a com. package comprising said combination. Thus, the effects of 5,6-dimethylxanthenone-4-acetic acid (Compound A), trastuzumab and paclitaxel are evaluated for their antitumor activity using the BT-474 human breast ductal carcinoma xenograft model; the data shows that Compound A at 20 mg/kg given i.v. on days 1, 5 and 9 is able to produce inhibition of tumor growth; paclitaxel combined with trastuzumab is also active resulting in a combination effect; when Compound A at 20 mg/kg is combined with paclitaxel and trastuzumab, increased activity is apparent resulting in tumor regressions; using the Clark Combination Index method, synergy is indicated; the tolerability of the triple combinations is no worse than that observed when Compound A is dosed alone.

L3 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1507331 CAPLUS
DOCUMENT NUMBER: 150:63975
TITLE: Mutual prodrugs comprising retinoids and histone deacetylase inhibitors, and methods to treat cancer
INVENTOR(S): Njar, Vincent C. O.; Gediya, Lalji K.; Khandelwal, Aakanksha
PATENT ASSIGNEE(S): University of Maryland, Baltimore, USA
SOURCE: PCT Int. Appl., 78pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008154372	A1	20081218	WO 2008-US66103	20080606

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,
FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2007-924932P P 20070606
US 2007-924995P P 20070607

OTHER SOURCE(S): MARPAT 150:63975

AB Mutual prodrugs comprising retinoids and histone deacetylase inhibitors, methods for production of the mutual prodrugs,

and methods of treatment comprising administration of the mutual prodrugs are disclosed. The retinoids include all-trans retinoic acid, 13-cis-retinoic acid, and retinoic acid analogs that have a substitution at C-4. Further, the mutual prodrugs of the present invention can be used as therapeutic agents for the treatment of cancer and dermatol. diseases and conditions. Pharmaceutical compns. comprising the mutual prodrugs are also disclosed. Thus, in the examples, the synthesis schemes of five mutual prodrugs, VNLG/60, VNLG/66, VNLG/114, VNLG/122, and VNLG/124, are provided. Further, all the mutual prodrugs were hydrolyzed in mice plasma at one hour into individual drugs (retinoids and histone deacetylase inhibitors) confirming that these mutual prodrugs are bioreversible.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:475762 CAPLUS

DOCUMENT NUMBER: 148:441007

TITLE: The use of a DNA damaging agent and a ligand for the treatment of cancer

INVENTOR(S): Brown, Michael Paul; Al-Ejeh, Fares; Darby, Jocelyn Margaret

PATENT ASSIGNEE(S): Medvet Science Pty. Ltd., Australia

SOURCE: PCT Int. Appl., 223pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008043148	A1	20080417	WO 2007-AU1543	20071011
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2007306927	A1	20080417	AU 2007-306927	20071011
CA 2666184	A1	20080417	CA 2007-2666184	20071011
EP 2073899	A1	20090701	EP 2007-815348	20071011
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				

PRIORITY APPLN. INFO.: US 2006-851213P P 20061011
WO 2007-AU1543 W 20071011

AB The present invention relates generally to a method of treating a neoplastic condition and to agents useful for same. More particularly, the present invention is directed to a method of facilitating the treatment of a metastatic neoplastic tumor in a localized manner by effecting the exposure of neoplastic cell intra-cellular mols., preferably intra-nuclear mols., suitable for use as a therapeutic target. The co-localization of tumor cells and metastases to discrete tissue locations thereby renders the method of the present invention useful in terms of the delivery of bystander-based therapy.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:11867 CAPLUS
DOCUMENT NUMBER: 148:106222
TITLE: Pharmaceutical compositions containing inhibitors of histone deacetylase and B vitamins, and methods of use thereof in the treatment of histone deacetylase dependent diseases
INVENTOR(S): Shultz, Michael
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2008002862	A1	20080103	WO 2007-US72004		20070625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2007265190	A1	20080103	AU 2007-265190		20070625
CA 2660782	A1	20080103	CA 2007-2660782		20070625
EP 2034978	A1	20090318	EP 2007-798994		20070625
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS					
IN 2008DN10353	A	20090320	IN 2008-DN10353		20081215
MX 2008016125	A	20090115	MX 2008-16125		20081216
KR 2009023631	A	20090305	KR 2008-731346		20081224
CN 101478959	A	20090708	CN 2007-80024079		20081226
PRIORITY APPLN. INFO.:			US 2006-816459P	P	20060626
			WO 2007-US72004	W	20070625

AB The invention relates to pharmaceutical compns. containing inhibitors of histone deacetylase and B vitamins and methods of use thereof, in the treatment of histone deacetylase (HDAC) dependent diseases and for the manufacture of pharmaceutical prepns. for the treatment of said diseases. Thus, the combination therapy of the HDAC inhibitor and the B vitamin mol. was found to more greatly inhibit tumor growth, i.e. reduction in tumor size, tumor weight, tumor number, and tumor perfusion, in comparison to the results obtained from administration of the single agent, i.e., only the HDAC inhibitor.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:413940 CAPLUS
DOCUMENT NUMBER: 149:700

TITLE: Improved synthesis of histone deacetylase inhibitors (HDIs) (MS-275 and CI-994) and inhibitory effects of HDIs alone or in combination with RAMBAs or retinoids on growth of human LNCaP prostate cancer cells and tumor xenografts
AUTHOR(S): Gediya, Lalji K.; Belosay, Aashvini; Khandelwal, Aakanksha; Purushottamachar, Puranik; Njar, Vincent C. O.
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD, 21201-1559, USA
SOURCE: Bioorganic & Medicinal Chemistry (2008), 16(6), 3352-3360
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 149:700
AB We have developed new, simple, and efficient procedures for the synthesis of two promising histone deacetylase inhibitors (HDIs), CI-994, (N-(2-aminophenyl)-4-acetylaminobenzamide), and MS-275 (N-(2-aminophenyl)4-[N-(pyridine-3-yl-methoxycarbonyl)aminomethyl]benzamide) from com. available acetamidobenzoic acid and 3-(hydroxymethyl)pyridine, resp. The procedures provide CI-994 and MS-275 in 80% and 72% overall yields, resp. We found that the combination of four HDIs (CI-994, MS-275, SAHA, and TSA) with retinoids all-trans-retinoic acid (ATRA) or 13-cis-retinoic acid (13-CRA) or our atypical retinoic acid metabolism blocking agents (RAMBAs) 1 (VN/14-1) or 2 (VN/66-1) produced synergistic anti-neoplastic activity on human LNCaP prostate cancer cells. The combination of 2 and SAHA induced G1 and G2/M cell cycle arrest and a decrease in the S phase in LNCaP cells. 2 + SAHA treatment effectively down-regulated cyclin D1 and cdk4, and up-regulated pro-differentiation markers cytokeratins 8/18 and pro-apoptotic Bad and Bax. Following s.c. administration, 2, SAHA or 2 + SAHA were well tolerated and caused significant suppression/regression of tumor growth compared with control. These results demonstrate that compound 2 and its combination with SAHA are potentially useful agents that warrant further preclin. development for treatment of prostate cancer.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1146835 CAPLUS
DOCUMENT NUMBER: 147:455453
TITLE: Combination chemotherapy containing Bcr-abl animal genes and c-Kit and PDGF-R tyrosine kinase inhibitors for treating cancer
INVENTOR(S): Burke, Gregory Peter; Linnartz, Ronald Richard; Manley, Paul W.; Versace, Richard William
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2007115289	A2	20071011	WO 2007-US65916	20070406
WO 2007115289	A3	20080410		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

CA 2644143	A1	20071011	CA 2007-2644143	20070404
AU 2007234382	A1	20071011	AU 2007-234382	20070406
JP 2009532499	T	20090910	JP 2009-504436	20070406
EP 2012787	A2	20090114	EP 2007-781287	20080407

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS

IN 2008DN07495	A	20080926	IN 2008-DN7495	20080903
US 20090233905	A1	20090917	US 2008-294208	20080923
MX 2008012728	A	20081014	MX 2008-12728	20081002
CN 101415424	A	20090422	CN 2007-80012017	20081006
KR 2008109068	A	20081216	KR 2008-727023	20081104

PRIORITY APPLN. INFO.:	US 2006-789403P	P	20060405
	WO 2007-US65916	W	20070406

OTHER SOURCE(S): MARPAT 147:455453

AB The invention relates to a combination comprising a Bcr-Abl, c-Kit and PDGF-R tyrosine kinase inhibitor; and one or more pharmaceutically active agents; pharmaceutical compns. comprising said combination; methods of treatment comprising said combination; processes for making said combination; and a com. package comprising said combination.

L3 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:561763 CAPLUS
DOCUMENT NUMBER: 146:494108
TITLE: Anti-angiogenic activity of 2-methoxyestradiol in combination with anti-cancer agents
INVENTOR(S): Plum, Stacy M.; Strawn, Steven J.; Lavallee, Theresa M.; Sidor, Carolyn F.; Fogler, William E.; Treston, Anthony M.
PATENT ASSIGNEE(S): Entremed, Inc., USA
SOURCE: PCT Int. Appl., 49pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007059111	A2	20070524	WO 2006-US44152	20061114
WO 2007059111	A3	20090514		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,

TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 20070185069 A1 20070809 US 2006-599997 20061114
PRIORITY APPLN. INFO.: US 2005-736220P P 20051114
US 2006-788354P P 20060331

AB The present invention relates generally to methods and compns. of treating disease characterized by abnormal cell proliferation and/or abnormal or undesirable angiogenesis by administering antiangiogenic agents in combination with chemotherapeutic agents. More specifically, the present invention relates to a methods and compns. of treating diseases characterized by abnormal cell proliferation and/or abnormal or undesirable angiogenesis by administering 2-methoxyestradiol, in combination with chemotherapeutic agents.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L3 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:724805 CAPLUS
DOCUMENT NUMBER: 147:180653
TITLE: Histone deacetylase inhibitor, suberoylanilide hydroxamic acid (Vorinostat, SAHA) profoundly inhibits the growth of human pancreatic cancer cells
AUTHOR(S): Kumagai, Takashi; Wakimoto, Naoki; Yin, Dong; Gery, Sigal; Kawamata, Norihiko; Takai, Noriyuki; Komatsu, Naoki; Chumakov, Alexy; Imai, Yasufumi; Koeffler, H. Phillip
CORPORATE SOURCE: Division of Hematology/Oncology, Cedars-Sinai Medical Center, UCLA School of Medicine, Los Angeles, CA, USA
SOURCE: International Journal of Cancer (2007), 121(3), 656-665
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tumor suppressor genes are often silenced in human cancer; this can occur by transcriptional repression by deacetylation in the promoter regions, mediated by histone deacetylase (HDAC). HDAC inhibitors can block cancer cell growth by restoring expression of tumor suppressor genes. In this study, we investigated the effects of a HDAC inhibitor, suberoylanilide hydroxamic acid (SAHA) on pancreatic cancer cells. SAHA inhibited the growth of 6 pancreatic cancer cell lines in a dose-dependent manner as measured by MTT and clonogenic assays (ED50 ≈10-6 M) associated with induction of apoptosis, G2 cell cycle arrest and also induced differentiation as indicated by morphol. and increased expression of cytokeratin 7. It increased expression of p21WAF1 (independent of the mutational status of p53), C/EBPα, RARα and E-cadherin; these genes have been associated with decreased proliferation in other cancers. SAHA decreased cyclin B1 expression; this cyclin normally promotes progression through G2 of the cell cycle. SAHA mediated acetylation of histone H3 globally, as well as, associated with the p21WAF1 promoter, as measured by chromatin immunopptn. SAHA also decreased levels of c-myc and cyclin D1, independent of an active β-catenin pathway. In further studies, the combination of SAHA and an inhibitor of DNA methylation, 5-Aza-2'-deoxycytidine, had an enhanced antiproliferative effect on pancreatic cancer cells. In summary, SAHA inhibited the growth of human pancreatic cancer cells by inducing apoptosis, differentiation and cell cycle arrest, as well as increase in the expression of several

tumor suppressor genes. SAHA is a novel, promising therapeutic agent for human pancreatic cancers.

OS.CITING REF COUNT: 26 THERE ARE 26 CAPLUS RECORDS THAT CITE THIS RECORD (26 CITINGS)

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 20 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007521337 EMBASE

TITLE: Vorinostat in cutaneous T-cell lymphoma.

AUTHOR: Duvic, Madeleine, Dr. Prof. (correspondence); Vu, Jenny

CORPORATE SOURCE: University of Texas, M.D. Anderson Cancer Center, Houston, TX, United States. mduvic@mdanderson.org

AUTHOR: Duvic, Madeleine, Dr. Prof. (correspondence)

CORPORATE SOURCE: Department of Dermatology, M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, United States. mduvic@mdanderson.org

SOURCE: Drugs of Today, (Sep 2007) Vol. 43, No. 9, pp. 585-599. Refs: 66
ISSN: 1699-4019 CODEN: MDACAP

COUNTRY: Spain

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 16 Nov 2007
Last Updated on STN: 16 Nov 2007

AB Histone deacetylase inhibitors (HDAC-Is) are a novel class of small molecules being evaluated in clinical trials for a number of different malignancies. HDAC-Is are able to induce differentiation, apoptosis and/or cell cycle arrest of malignant cells selectively. Vorinostat (Zolinza®, Merck & Co., Whitehouse Station, NJ, USA) is the first HDAC-I approved by the U.S. Food and Drug Administration for treatment of the cutaneous manifestations in patients with cutaneous T-cell lymphoma (CTCL) who have progressive, persistent or recurrent disease on or following two systemic therapies. Vorinostat was active against solid tumors and hematologic malignancies as intravenous and oral preparations in phase I development. In two phase II trials, Vorinostat was safe and effective at an oral dose of 400 mg/day with an overall response rate of 30-31% in refractory advanced patients with CTCL including large cell transformation and Sezary syndrome. The most frequent side effects of vorinostat include gastrointestinal symptoms, fatigue and thrombocytopenia. Vorinostat, in combination with other agents such as radiation therapy and chemotherapy, can have synergistic or additive effects in a variety of cancers in clinical trials. .COPYRGT. 2007 Prous Science. All rights reserved.

L3 ANSWER 10 OF 20 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007395467 EMBASE

TITLE: Epigenetic gene silencing in cancer: The DNA hypermethylome.

AUTHOR: Esteller, Manel (correspondence)

CORPORATE SOURCE: Cancer Epigenetics Laboratory, Spanish National Cancer Centre (CNIO), Melchor Fernandez Almagro 3, 28029 Madrid, Spain. mesteller@cnio.es

SOURCE: Human Molecular Genetics, (15 Apr 2007) Vol. 16, No. R1,

pp. R50-R59.
Refs: 99
ISSN: 0964-6906; E-ISSN: 1460-2083 CODEN: HMGEE5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
022 Human Genetics
025 Hematology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Sep 2007
Last Updated on STN: 7 Sep 2007

AB Epigenetic gene inactivation in transformed cells involves many 'belts of silencing'. One of the best-known lesions of the malignant cell is the transcriptional repression of tumor-suppressor genes by promoter CpG island hypermethylation. We are in the process of completing the molecular dissection of the entire epigenetic machinery involved in methylation-associated silencing, such as DNA methyltransferases, methyl-CpG binding domain proteins, histone deacetylases , histone methyltransferases, histone demethylases and Polycomb proteins. The first indications are also starting to emerge about how the combination of cellular selection and targeted pathways leads to abnormal DNA methylation. One thing is certain already, promoter CpG island hypermethylation of tumor-suppressor genes is a common hallmark of all human cancers. It affects all cellular pathways with a tumor-type specific profile, and in addition to classical tumor-suppressor and DNA repair genes, it includes genes involved in premature aging and microRNAs with growth inhibitory functions. The importance of hypermethylation events is already in evidence at the bedside of cancer patients in the form of cancer detection markers and chemotherapy predictors, and in the approval of epigenetic drugs for the treatment of hematological malignancies. In the very near future, the synergy of candidate gene approaches and large-scale epigenomic technologies, such as methyl-DIP, will yield the complete DNA hypermethylome of cancer cells.

L3 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:710800 CAPLUS
DOCUMENT NUMBER: 145:167105
TITLE: Preparation of novel pyrrolodihydroisoquinolines as inhibitors of cellular proliferation and inducers of apoptosis in cancer cells
INVENTOR(S): Vennemann, Matthias; Baer, Thomas; Braunger, Juergen; Gekeler, Volker; Gimmnich, Petra; Ciapetti, Paola; Contreras, Jean-Marie; Wermuth, Camille Georges
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006075012	A2	20060720	WO 2006-EP50165	20060111
WO 2006075012	A3	20061026		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

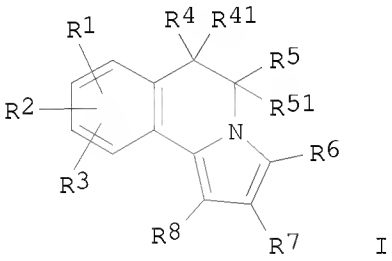
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2006205797	A1	20060720	AU 2006-205797		20060111
CA 2595075	A1	20060720	CA 2006-2595075		20060111
EP 1838708	A2	20071003	EP 2006-707703		20060111
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU					
JP 2008526817	T	20080724	JP 2007-549914		20060111
US 20080064714	A1	20080313	US 2007-794494		20070816
PRIORITY APPLN. INFO.:			EP 2005-100155	A	20050112
			WO 2006-EP50165	W	20060111

OTHER SOURCE(S): CASREACT 145:167105; MARPAT 145:167105

GI



I

AB The title compds. I [R1 = halo, NO2, NH2, etc.; R2 = H, halo, alkoxy; R3 = H, alkoxy; or R2 and R3 together form alkylenedioxy bridge; or R1 and R2 together form alkylenedioxy bridge and R3 = H; R4, R41 = H, alkyl; R5, R51 = H; R6 = alkyl or alkyl substituted by R61; R61 = alkoxycarbonyl, carboxyl; R7 = Ph, naphthyyl, etc.; R8 = C(O)R9; R9 = alkyl, cycloalkyl, cycloalkylalkyl or phenylalkyl] which are efficacious inhibitors of cellular (hyper)proliferation and/or inducers of apoptosis in cancer cells, were prepared Thus, reacting 1-(6,7-dimethoxy-3,4-dihydro-2H-isoquinolin-1-ylidene)butan-2-one (preparation given) with nitroethane and 4-hydroxy-3,5-dimethylbenzaldehyde afforded 1-[2-(4-hydroxy-3,5-dimethylphenyl)-8,9-dimethoxy-3-methyl-5,6-dihydro-pyrrolo[2,1-a]isoquinolin-1-yl]propan-1-one which showed -logIC50 in the range from 5.8 to 6.8 when tested on NCI-H460 non-small cell lung cancer cells. Pharmaceutical formulations comprising the compound I alone or in combination with other therapeutic agents are disclosed.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 20 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006011079 EMBASE

TITLE: The histone deacetylase (HDAC) inhibitor valproic acid as monotherapy or in combination

with all-trans retinoic acid in patients with acute myeloid leukemia.
AUTHOR: Kuendgen, Andrea, Dr. (correspondence); Knipp, Sabine; Germing, Ulrich; Haas, Rainer; Gattermann, Norbert
CORPORATE SOURCE: Department of Hematology, Oncology, and Clinical Immunology, Heinrich-Heine-University, Moorenstr. 5, D-40225 Dusseldorf, Germany. kuendgen@med.uni-duesseldorf.de
AUTHOR: Schmid, Mathias; Schlenk, Richard; Dohner, Hartmut
CORPORATE SOURCE: Third Department of Internal Medicine, University of Ulm, Ulm, Germany.
AUTHOR: Hildebrandt, Barbara
CORPORATE SOURCE: Institute of Human Genetics, Heinrich-Heine-University, Dusseldorf, Germany.
AUTHOR: Steidl, Christian
CORPORATE SOURCE: Department of Hematology/Oncology, University of Gottingen, Gottingen, Germany.
SOURCE: Cancer, (1 Jan 2006) Vol. 106, No. 1, pp. 112-119.
Refs: 43
ISSN: 0008-543X CODEN: CANCAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jan 2006
Last Updated on STN: 26 Jan 2006

AB BACKGROUND. Valproic acid (VPA) inhibits histone deacetylase activity and, synergizing with all-trans retinoic acid (ATRA), achieves differentiation induction of myeloid blast cells in vitro. METHODS. We used VPA in 58 patients with acute myeloid leukemia (AML) who were too old and/or medically unfit to receive intensive chemotherapy (32 AML secondary to myelodysplastic syndrome [MDS], 22 de novo AML, 4 AML secondary to myeloproliferative syndrome). VPA serum concentrations were 50-100 μg/mL. Thirty-one patients received VPA monotherapy. ATRA was added later in 13 patients who did not respond or who relapsed. Another 27 patients received VPA plus ATRA from the start. Median treatment duration was 93 days for VPA and 88 days for ATRA. RESULTS. The response rate was only 5% according to International Working Group (IWG) criteria for AML but was 16% when IWG response criteria for MDS were used, which capture hematologic improvement and stabilization of the disease. These endpoints, which are not necessarily correlated with diminishing blast counts, are relevant for the patients' quality of life. Among 23 patients with a peripheral blast count > 5%, 6 (26%) showed a diminishing blast count, and 5 of these had a complete peripheral blast clearance. CONCLUSIONS. Future trials should combine VPA with chemotherapy or demethylating agents. .COPYRGT. 2005 American Cancer Society.

L3 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:232565 CAPLUS
DOCUMENT NUMBER: 142:309871
TITLE: Combination methods of treating cancer
INVENTOR(S): Bacopoulos, Nicholas G.; Chiao, Judy H.; Marks, Paul A.; Miller, Thomas A.; Paradise, Carolyn M.; Richon, Victoria M.; Rifkind, Richard A.
PATENT ASSIGNEE(S): Aton Pharma, Inc., USA; Sloan-Kettering Institute for Cancer Research
SOURCE: PCT Int. Appl., 134 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023179	A2	20050317	WO 2004-US26161	20040812
WO 2005023179	A3	20050616		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004270150	A2	20050317	AU 2004-270150	20040812
AU 2004270150	A1	20050317		
CA 2535889	A1	20050317	CA 2004-2535889	20040812
EP 1667680	A2	20060614	EP 2004-780925	20040812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007504131	T	20070301	JP 2006-524699	20040812
CN 1964714	A	20070516	CN 2004-80031561	20040812
IN 2006DN00897	A	20070810	IN 2006-DN897	20060221
US 20070190022	A1	20070816	US 2007-567953	20070103
PRIORITY APPLN. INFO.:			US 2003-498803P P	20030829
			WO 2004-US26161 W	20040812

OTHER SOURCE(S): MARPAT 142:309871

AB The present invention relates to a method of treating cancer in a subject in need thereof, by administering to a subject in need thereof a first amount of a histone deacetylase (HDAC) inhibitor or a pharmaceutically acceptable salt or hydrate thereof, in a first treatment procedure, and a second amount of an anti-cancer agent in a second treatment procedure. The first and second amts. together comprise a therapeutically effective amount The effect of the HDAC inhibitor and the anti-cancer agent may be additive or synergistic.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1081068 CAPLUS
DOCUMENT NUMBER: 142:51881
TITLE: Systems, methods and kits for characterizing phosphoproteomes by digestion, chromatography and mass spectrometry
INVENTOR(S): Gygi, Steven P.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108948	A2	20041216	WO 2004-US17613	20040604
WO 2004108948	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20050164324	A1	20050728	US 2004-862195	20040604
PRIORITY APPLN. INFO.:			US 2003-476010P P	20030604

AB The invention provides systems, software, methods and kits for detecting and/or quantifying phosphorylatable polypeptides and/or acetylated polypeptides in complex mixts., such as a lysate of a cell or cellular compartment (e.g., such as an organelle). The methods can be used in high throughput assays to profile phosphoproteomes and to correlate sites and amts. of phosphorylation with particular cell states.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:965067 CAPLUS
DOCUMENT NUMBER: 141:406039
TITLE: Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis
INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A.
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424
WO 2004096224	A3	20041216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1473043	A1	20041103	EP 2003-9587	20030429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

AU 2004233576	A1	20041111	AU 2004-233576		20040424
CA 2523868	A1	20041111	CA 2004-2523868		20040424
EP 1622619	A2	20060208	EP 2004-729366		20040424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
BR 2004009919	A	20060425	BR 2004-9919		20040424
JP 2006524634	T	20061102	JP 2006-500099		20040424
IN 2005DN04018	A	20091002	IN 2005-DN4018		20050907
MX 2005011656	A	20051215	MX 2005-11656		20051028
NO 2005005605	A	20051128	NO 2005-5605		20051128
PRIORITY APPLN. INFO.:			EP 2003-9587	A	20030429
			EP 2004-508	A	20040113
			EP 2004-1171	A	20040121
			WO 2004-EP4363	W	20040424

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:1154310 CAPLUS

DOCUMENT NUMBER: 142:69220

TITLE: Topical use of valproic acid, alone or with other agents, for the prevention or treatment of skin disorders

INVENTOR(S): Pelicci, Pier Giuseppe; Minucci, Saverio; Costanzo, Antonio; Chimenti, Sergio; Nistico, Steven Paul; Paolino, Donatella

PATENT ASSIGNEE(S): G2M Cancer Drugs AG, Germany

SOURCE: Eur. Pat. Appl., 40 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1491188	A1	20041229	EP 2003-14278	20030625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004251434	A1	20050106	AU 2004-251434	20040623
AU 2004251435	A1	20050106	AU 2004-251435	20040623
CA 2531101	A1	20050106	CA 2004-2531101	20040623
CA 2531107	A1	20050106	CA 2004-2531107	20040623
WO 2005000289	A1	20050106	WO 2004-EP6789	20040623
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2005000282	A2	20050106	WO 2004-EP6797	20040623
WO 2005000282	A3	20050428		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1635808	A1	20060322	EP 2004-740209	20040623
EP 1635808	B1	20081001		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

EP 1635798	A2	20060322	EP 2004-740216	20040623

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

JP 2008529964	T	20080807	JP 2006-516036	20040623
JP 2008529966	T	20080807	JP 2006-516039	20040623
AT 409471	T	20081015	AT 2004-740209	20040623
ES 2310734	T3	20090116	ES 2004-740209	20040623
EP 2039355	A2	20090325	EP 2008-13246	20040623

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

US 20060160897	A1	20060720	US 2005-275258	20051221
US 20070037738	A1	20070215	US 2005-275263	20051221

PRIORITY APPLN. INFO.:	EP 2003-14278	A	20030625
	EP 2004-740209	A3	20040623
	WO 2004-EP6789	W	20040623
	WO 2004-EP6797	W	20040623

OTHER SOURCE(S): MARPAT 142:69220

AB The invention relates to a topically applicable formulation containing valproic acid or a derivative thereof which can be used alone or in combination with topically applicable formulations of retinoids or of nuclear receptor ligands, or of chemotherapeutic agents (e.g. 5-Fluorouracil). The formulation is useful for the topical treatment of cancerous skin disorders, e.g. basal cell carcinoma, squamous cell carcinoma, keratoakantoma, Bowen disease, cutaneous T-Cell lymphoma, and also for the topical treatment of premalignant lesions, and of inflammation of the skin and/or mucosa. The invention also relates to the use of this topically applicable formulation for protection from UV light and for the treatment of sunburn. The invention includes the use of valproic acid for the manufacture of a clin. used medicament for the topical treatment of the above human diseases.

OS.CITING REF COUNT:	5	THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT:	11	THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 20 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:477875 BIOSIS

DOCUMENT NUMBER: PREV200510269779
TITLE: Phase 2 trial of the histone deacetylase inhibitor valproic acid as a monotherapy or in combination with all-trans retinoic acid in 24 patients with acute myeloid leukemia.
AUTHOR(S): Kuendgen, Andrea [Reprint Author]; Strupp, Corinna; Hildebrandt, Barbara; Knipp, Sabine; Junge, Baerbel; Haas, Rainer; Germing, Ulrich; Gattermann, Norbert
CORPORATE SOURCE: Univ Dusseldorf, D-4000 Dusseldorf, Germany
SOURCE: Blood, (NOV 16 2004) Vol. 104, No. 11, Part 1, pp. 501A. Meeting Info.: 46th Annual Meeting of the American-Society-of-Hematology. San Diego, CA, USA. December 04 -07, 2004. Amer Soc Hematol. CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005
AB Valproic acid (VPA) has been shown to inhibit historic deacetylase activity, and to synergize with ATRA in the differentiation induction of leukemic myeloidblast cells in vitro. We applied VPA to 20 patients (16 sAML/ MDS, 2 de-novo-AML, 2 sAML/OMF) too old or physically unfit to receive intensive chemotherapy. VPA monotherapy was targeted to reach serum concentrations of 50-100mg/ml. ATRA was added (80mg/m2/d in two divided doses, every other week) in some of the patients who did not respond or who relapsed. To enhance responses, we treated an additional 4 patients (2 sAML/MDS, 1 sAML/ET, I de novo AML) with VPA+ATRA from the start. Median age was 70 years (51-84). Median bone marrow blast count was 30% (10-80). 5 patients had only 10-15% marrow blasts but were included because they showed treatment failure or relapse after chemotherapy and were unable to receive further cytotoxic treatment. Median treatment duration was99 days (20396) for VPA and 79 days (18-339) for ATRA. Responses according tointernational working group (IWG, Cheson et al., 2003) criteria were observedin 5 patients (25%) on VPA monotherapy (4PR, 1CR). Of the responding patientstwo have ongoing responses (CR, PR) for 12 and 13 months, respectively. I patient reaching PR discontinued VPA when her physical condition had improved sufficiently to allow further chemotherapy. I patient relapsed after 2 months andwas switched to VPA+ATRA, without response. I patient died of infectious complications. 8 additional patients showed stable disease without increases in peripheral blast count. Responses lasted for a median of 4 months (2-13). Among the 4 patients receiving VPA+ATRA from the start, 1 (25%) achieved PR. When hestopped VPA after 3 months because of side effects, he continued oil ATRA, achieving a CRi (CR with incomplete recovery of platelets) lasting for 8 months.4 of 14 nonresponders were switched to VPA+ATRA, but none of them showed a response. Response to VPA treatment was not associated with FAB subtype or karyotype. Median bone marrow blast count was 28 (13-45)% in responders, 30 (10-75)% in patients with stable and 41 (25-80)% in patients with progressive disease. Since our patients mainly had secondary AML, we also analyzed our results according to the proposals of the IWG for MDS (Cheson et al., 2000). Among patients receiving VPA monotherapy I patient had a major trilineage response. 2 patients showed a minor erythroid and one a minor neutrophil response. In the second group of patients one had a major erythroid response. Concerning side effects, VPA caused tremor in four cases, leading to cessation of treatment in two. Regarding ATRA, grade 1-2 skin toxicity was observed in 4, grade 1-2 gastrointestinal toxicity in 2, and pleural effusion in I patient. In summary, we observed responses according to IWG criteria in 25% of our patients (6/24). The best responses to VPA or VPA+ATRA in AML patients occurred in patients with lowblast count, mainly in patients who showed relapsed or refractory disease shortly after intensive chemotherapy.

These data indicate that VPA might be most effectively applied after or in addition to intensive chemotherapy.

L3 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:219666 CAPLUS
DOCUMENT NUMBER: 138:231716
TITLE: Valproic acid and derivatives thereof for the combination therapy of human cancers, for the treatment of tumor metastasis and minimal residual disease
INVENTOR(S): Heinzel, Thorsten; Gottlicher, Martin; Hentsch, Bernd; Wels, Winfried Stephan; Pelicci, Pier Giuseppe; Minucci, Saverio; Herrlich, Peter A.; Groner, Bernd
PATENT ASSIGNEE(S): G2M Cancer Drugs AG, Germany
SOURCE: Eur. Pat. Appl., 61 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1293205	A1	20030319	EP 2001-121722	20010918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2460713	A1	20030327	CA 2002-2460713	20020917
WO 2003024442	A2	20030327	WO 2002-EP10419	20020917
WO 2003024442	A3	20030918		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002338716	A1	20030401	AU 2002-338716	20020917
AU 2002338716	B2	20070816		
EP 1427403	A2	20040616	EP 2002-777129	20020917
EP 1427403	B1	20051228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
EP 1529527	A2	20050511	EP 2005-101081	20020917
EP 1529527	A3	20050525		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
JP 2005512961	T	20050512	JP 2003-528538	20020917
EP 1602371	A2	20051207	EP 2005-19659	20020917
EP 1602371	A3	20061115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
AT 314063	T	20060115	AT 2002-777129	20020917
ES 2252519	T3	20060516	ES 2002-777129	20020917
US 20050038113	A1	20050217	US 2004-489770	20041029
AU 2007207869	A1	20070906	AU 2007-207869	20070816
AU 2007207869	B2	20090910		

PRIORITY APPLN. INFO.:		
EP 2001-121722	A	20010918
AU 2002-338716	A3	20020917
EP 2002-777129	A3	20020917

WO 2002-EP10419 W 20020917

OTHER SOURCE(S): MARPAT 138:231716

AB The invention discloses the use of valproic acid and derivs. thereof as inhibitors of enzymes having histone deacetylase activity for the therapeutic treatment of human cancers in combination with established therapeutic principles. The invention also discloses the use of these compds. for the treatment of tumor metastasis and minimal residual disease. The invention includes the manufacture of a clin. used substance for the treatment of human cancers.

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 20 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003463397 EMBASE

TITLE: Fenretinide: A prototype cancer prevention drug.

AUTHOR: Malone, Winfred; Perloff, Marjorie; Crowell, James (correspondence)

CORPORATE SOURCE: National Cancer Institute, Division of Cancer Prevention, Chemoprev. Agent Devmt. Res. Group, Bethesda, MD, United States.

AUTHOR: Sigman, Caroline; Higley, Howard

CORPORATE SOURCE: CCS Associaties, 2005 Landings Drive, Mountain View, CA 94043, United States.

SOURCE: Expert Opinion on Investigational Drugs, (Nov 2003) Vol. 12, No. 11, pp. 1829-1842.
Refs: 150
ISSN: 1354-3784 CODEN: EOIDER

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 1 Dec 2003
Last Updated on STN: 1 Dec 2003

AB Fenretinide (N-4-hydroxyphenylretinamide [4-HPR]) is a synthetic retinoid that has been examined in in vitro assays, preclinical animal models and clinical trials as a cancer chemopreventive agent. Its pharmacology, toxicity and mechanisms of action initially suggested an increased therapeutic index relative to native retinolds for the control of tumours of the breast, prostate, bladder, colon, cervix and head and neck. Although fenretinide at the doses and schedules used in several pivotal Phase II and III clinical trials has not been proven to be efficacious in reducing the incidence of cancer or in retarding the development of preneoplastic lesions, encouraging observations regarding unanticipated preventative activity, such as for ovarian cancer control, have arisen from these studies. Research in cancer therapy and the elucidation of molecular pathways activated by fenretinide have also yielded clues about how this agent might be better used in a prevention setting. Current trials are underway to re-examine both dose and schedule of fenretinide administration as well as the target tissues of interest. Investigations of potential synergism between fenretinide and other candidate chemopreventative molecules with complementary mechanisms of action may support future assessments of this prototype cancer prevention drug or its newer analogues.

L3 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:594666 CAPLUS
DOCUMENT NUMBER: 137:135074
TITLE: Use of retinoids plus histone deacetylase inhibitors to inhibit the growth of solid tumors
INVENTOR(S): Gudas, Lorraine J.; Nanus, David
PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002060430	A1	20020808	WO 2002-US2976		20020201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002242057	A1	20020812	AU 2002-242057		20020201
US 20020183388	A1	20021205	US 2002-61101		20020201
PRIORITY APPLN. INFO.:			US 2001-265651P	P	20010201
			WO 2002-US2976	W	20020201

AB The invention provides a method of inhibiting growth of solid tumors in an animal which comprises administering an effective amount of trichostatin A to an animal in need of such treatment. The invention also provides a method of inhibiting growth of solid tumors in an animal which comprises administering an effective amount of a histone deacetylase inhibitor and a retinoid to an animal in need of such treatment. Examples of solid tumors which may be treated using the methods of the invention include but are not limited to carcinomas of the head and neck, breast, skin, kidney, oral cavity, colon, prostate, pancreas and lung.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s retino? and (histone (s) deacetylase) and (epiderm? or keratin or transglutaminase?)
L4 143 RETINO? AND (HISTONE (S) DEACETYLASE) AND (EPIDERM? OR KERATIN OR TRANSGLUTAMINASE?)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 123 DUP REM L4 (20 DUPLICATES REMOVED)

=> s l5 and @py<=2005
'2005' NOT A VALID FIELD CODE
'2005' NOT A VALID FIELD CODE
'2005' NOT A VALID FIELD CODE
'2005' NOT A VALID FIELD CODE
L6 0 L5 AND @PY<=2005

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=> s l5 and py<=2005
L7          65 L5 AND PY<=2005

=> d l7 ibib abs 1-65

L7   ANSWER 1 OF 65  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2008:490349  CAPLUS
DOCUMENT NUMBER:         148:441008
TITLE:                   One-step epigenetic switch cancer model and methods of
                         diagnosis and therapy targeted against cancer stem
                         line
INVENTOR(S):             Bergstein, Ivan
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S., 43pp., Cont.-in-part of U.S. Ser. No. 933,330.
                         CODEN: USXXAM
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  3
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
     US 7361336           B1    20080422    US 1999-468286          19991220
     US 6004528           A     19991221    US 1997-933330          19970918 <--
     US 20060083682       A1    20060420    US 2005-271381          20051110
     US 20070036800       A1    20070215    US 2006-583744          20061018
     US 7608259           B2    20091027
     US 20070036801       A1    20070215    US 2006-583841          20061018
     US 7504103           B2    20090317
     US 20070036802       A1    20070215    US 2006-583857          20061018
     US 7427400           B2    20080923
     US 20070036803       A1    20070215    US 2006-583860          20061018
     US 20070036804       A1    20070215    US 2006-583871          20061018
     US 20080305107       A1    20081211    US 2008-187221          20080806
     US 20090011441       A1    20090108    US 2008-187177          20080806
     US 20090022740       A1    20090122    US 2008-187205          20080806
     US 20090022741       A1    20090122    US 2008-187240          20080806
     US 20090028878       A1    20090129    US 2008-187198          20080806
     US 20090028879       A1    20090129    US 2008-187232          20080806
PRIORITY APPLN. INFO.:                       US 1997-933330      A2 19970918
                                             US 1999-468286      A1 19991220
                                             US 2005-271381      A1 20051110
                                             US 2006-583744      A1 20061018

AB   The present invention provides novel methods for the treatment and
     detection of cancer which follow from the OSES model of carcinogenesis.
     In brief, the OSES model concludes that a clandestine relatively
     mutationally-spared immortal founder line (i.e., cancer stem line) exists
     within tumors and is responsible for fueling tumor immortality.  Since the
     cancer stem line is directly derived from normal stem cells, the cancer
     stem line (like a normal stem cell) is slow-growing and non-mutant and
     (like a normal stem cell) rears a transit population of highly
     proliferative progeny cells (which may be mutant in the case of cancer
     stem line progeny).  Such highly proliferative and largely mortal cancer
     stem line progeny make up the bulk of the resulting tumor mass (in an
     analogous manner to which proliferative mortal progeny of normal stem
     cells make up the bulk of a normal developing tissue).  Essentially, while
     conventional cancer models invoke the presence of highly proliferative
     mutant cancers (hypothesized to be produced by stepwise neo-Darwinian
     mutation-selection), they have been largely unaware of the OSES-iw
     proposed presence of an underlying slow-growing relatively
     mutationally-spared immortal cancer stem line that rears such
     proliferative mutant cells as its mortal progeny.  Moreover, this
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deficiency by conventional models explains many of the inadequacies of treatment regimens derived thereof, e.g., conventional chemotherapies, irradiation, exptl. immunotherapies, as well as newer gene-directed therapies designed for treatment of cancer. In general, such conventionally-based methods attempt to eradicate fast-growing mutant cancer cells. This idea has clin. utility as, if successful, such methods may destroy the highly proliferative mutant progeny of the cancer stem line and thereby diminish tumor burden (since mortal cancer stem line progeny make up the bulk of the tumor mass), thus potentially effecting clin. remission (due to significant decrease in tumor cell burden). However, a problem associated with such treatments is that the targeted highly proliferative mutant cancer cells are largely mortal while their immortal progenitor, i.e., the cancer stem line, will remain spared of such therapies. This is disadvantageous as the cancer stem line over time can rear more highly proliferative mutant cancer cells, thereby effecting an increase in tumor cell burden and clin. relapse. By contrast, the subject invention provides novel therapies which eradicate the slow-growing relatively mutationally-spared cancer stem line which is the progenitor of the larger population of highly proliferative, largely mortal, often mutant cancer cells. Therefore, the present invention may provide a true cancer cure as it would eradicate the founder line there by alleviating and potentially preventing clin. relapse. It is a more specific object of the invention to provide a method of cancer therapy which targets slow growing, relatively mutationally-spared sym. dividing stem cells (i.e., a cancer stem line) which is the immortal founder line that rears those (largely mortal) highly proliferative mutant cancer cells normally targeted by conventional therapies. It is another specific object of the invention to provide novel and improved cancer therapies which eradicate a cancer stem line thereby destroying the immortal portion of the tumor (i.e., the cancer stem line) and in doing so providing a true cure by preventing clin. relapse. It is a more specific object of the invention to provide cancer therapies which target antigens present on the cancer stem line for the purpose of destroying the cancer stem line. It is another specific object of the invention to provide a novel method of cancer therapy which induces, in a cancer stem line, a permanent switch from sym. to asym. mitosis. It is still another specific object of the invention to provide a novel method of cancer therapy which induces, in a cancer stem line, terminal differentiation and/or programmed cell death. It is still another specific object of the invention to spare normal stem cells of significant OSES-based therapy-induced toxicities.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:356698 CAPLUS
DOCUMENT NUMBER: 146:372833
TITLE: Histone deacetylase inhibitor or histone hyperacetylating agent for promoting wound healing and preventing scar formation
INVENTOR(S): Chung, Yih-Lin
PATENT ASSIGNEE(S): Taiwan
SOURCE: U.S. Pat. Appl. Publ., 36pp., Cont.-in-part of U.S. Ser. No. 205,738.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070072793	A1	20070329	US 2004-843025	20040510
US 20040018958	A1	20040129	US 2002-205738	20020725 <--
US 6809118	B2	20041026		
AT 400261	T	20080715	AT 2004-5807	20040311
ES 2311763	T3	20090216	ES 2004-5807	20040311
US 20060275370	A1	20061207	US 2006-499936	20060807
CA 2601999	A1	20090317	CA 2007-2601999	20070917
AU 2009202036	A1	20090611	AU 2009-202036	20090522
PRIORITY APPLN. INFO.:			US 2002-205738	A2 20020725
			EP 2004-5807	A 20040311
			US 2004-798119	A2 20040311
			US 2004-843025	A2 20040510
			AU 2007-214300	A3 20070829

AB The invention discloses a method for promoting wound healing and preventing scar formation in a variety of wounds in skin, mucosa, and cornea. The method comprises administering a therapeutically effective amount of a histone deacetylase inhibitor or a hyperacetylating agent. The histone deacetylase inhibitor or hyperacetylating agent is capable of stimulating multiple cytokines/growth factors in the early phase of wound healing, and suppressing fibrogenic cytokines/growth factors in the late phase of tissue remodeling in the wound site, and is useful in promoting epithelial cell regrowth and reducing excessive collagen accumulation, which results in rapid wound closure with reduced scaring.

L7 ANSWER 3 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:175142 CAPLUS
DOCUMENT NUMBER: 146:244322
TITLE: Novel methods of cancer diagnosis and therapy targeted against a cancer stem line
INVENTOR(S): Bergstein, Ivan
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46pp., Cont. of U.S. Ser. No. 468,286.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070036800	A1	20070215	US 2006-583744	20061018
US 7608259	B2	20091027		
US 6004528	A	19991221	US 1997-933330	19970918 <--
US 7361336	B1	20080422	US 1999-468286	19991220
US 20080305107	A1	20081211	US 2008-187221	20080806
US 20090022741	A1	20090122	US 2008-187240	20080806
US 20090028879	A1	20090129	US 2008-187232	20080806
PRIORITY APPLN. INFO.:			US 1997-933330	A2 19970918
			US 1999-468286	A1 19991220
			US 2006-583744	A1 20061018

AB Improved methods for treatment of cancer which involve the targeting of slow-growing, relatively mutationally-spared cancer stem line are provided. These methods are an improvement over previous cancer therapeutic methods because they provide for very early cancer treatment and reduce the likelihood of clin. relapse after treatment.

L7 ANSWER 4 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:683054 CAPLUS

DOCUMENT NUMBER: 146:395633
TITLE: Advances in studies of transcriptional regulation of hTERT gene
AUTHOR(S): Kong, Hong; Yu, Cheng-guo
CORPORATE SOURCE: Second Clinical College, China Medical University, Shenyang, 110006, Peop. Rep. China
SOURCE: Guowai Yixue Linchuang Shengwu Huaxue Yu Jianyanxue Fence (2005), 26(8), 526-529
CODEN: GYLSA5; ISSN: 1006-3730
PUBLISHER: Chongqing Shi Weisheng Xinxi Zhongxin
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. This article reviews the studies on the transcriptional regulation of hTERT genes. The paper described the current knowledge on the regulatory elements in the promoter region of hTERT gene. The paper also talks about the transcription factors including estrogen receptor, histone deacetylase and histone acetyltransferase and other factors involved in the regulation of hTERT gene. The regulation of hTERT gene is related to the telomere maintenance in normal cell proliferation and tumorigenesis of various cancers.

L7 ANSWER 5 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:605986 CAPLUS
DOCUMENT NUMBER: 145:77624
TITLE: Use of integrating exon-trapping reporter genes in the analysis of gene expression profiles in cells
INVENTOR(S): Link, Charles J.; Seregina, Tatiana; Vahanian, Nicholas N.; Higginbotham, James N.; Ramsey, William Jay; Powers, Bradley J.; Shukla, Sachet A.; Young, Won Bin; Dicolandrea, Teresa; Mautino, Mario R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 80 pp., Cont.-in-part of U.S. Ser. No. 811,842.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 20060134629	A1	20060622	US 2003-660893	20030912	
US 20010034028	A1	20011025	US 2001-811842	20010319	<--
US 6897020	B2	20050524			
WO 2005054476	A1	20050616	WO 2004-US29658	20040913	<--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 2000-190678P	P	20000320
US 2001-811842	A2	20010319
US 2003-458152P	P	20030327
US 2000-198722P	P	20000420
US 2003-660893	A	20030912

AB A method for analyzing patterns of gene expression and protein profiles

using promoterless or exon-trapping reporter genes is described. The method uses a promoterless reporter gene that is delivered using an integrating vector, such as a retroviral vector, to integrate into the genome of the cell of interest. Changes in levels of reporter activity under different conditions are used to characterize the gene expression profile and to identify genes that may be informative. The informative genes may be cloned and characterized.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L7 ANSWER 6 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1259318 CAPLUS
DOCUMENT NUMBER: 144:583
TITLE: Methods and compositions using selective cytokine inhibitory drugs for treatment and management of cancers and other diseases
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005112918	A1	20051201	WO 2004-US14002	20040505 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004319815	A1	20051201	AU 2004-319815	20040505 <--
CA 2565446	A1	20051201	CA 2004-2565446	20040505 <--
EP 1750697	A1	20070214	EP 2004-751398	20040505
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LT, LV, MK				
CN 1984651	A	20070620	CN 2004-80043534	20040505
BR 2004018801	A	20071016	BR 2004-18801	20040505
JP 2007536222	T	20071213	JP 2007-511328	20040505
MX 2006012698	A	20070214	MX 2006-12698	20061103
KR 2007011564	A	20070124	KR 2006-725517	20061204
US 20080267905	A1	20081030	US 2008-579351	20080612

PRIORITY APPLN. INFO.: WO 2004-US14002 A 20040505
OTHER SOURCE(S): MARPAT 144:583

AB Methods of treating, preventing and/or managing cancer as well as and diseases and disorders associated with, or characterized by, undesired angiogenesis are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug alone or in combination with a second active ingredient. The invention further relates to methods of reducing or avoiding adverse side effects associated with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy which comprise the administration of a selective cytokine inhibitory drug. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1177394 CAPLUS
DOCUMENT NUMBER: 143:452842
TITLE: Proliferation- and differentiation-modulating agents specific to E2F pathway and uses therefor in the treatment of and drug screening for squamous carcinoma
INVENTOR(S): Saunders, Nicholas Andrew
PATENT ASSIGNEE(S): Australia
SOURCE: U.S. Pat. Appl. Publ., 65 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20050245473	A1	20051103	US 2004-967648		20041015 <--
PRIORITY APPLN. INFO.:			US 2003-512010P	P	20031016

AB The present invention discloses the use of E2F pathway modulators and optionally a differentiation stimulus in methods for treating or preventing conditions associated with the deregulation of epithelial cell proliferation and differentiation and for diagnosing the presence or risk of developing such conditions. Specifically, the present invention demonstrates E2Fs 1-5 can suppress the activity of differentiation-specific markers using transglutaminase 1 gene promoter driven luciferase in primary human keratinocyte cell culture. The DNA binding domain and transactivation domain of E2F1 is essential for suppression of differentiation-specific marker activity. E2F is required for but not sufficient to induce squamous differentiation; inhibition of E2F in the presence of a differentiation-inducing agent reinstates TG-1 Luc activity in a squamous cell carcinoma cell line. Thus E2F acts as a modulator of the keratinocyte differentiation and the targeted disruption of E2F-1 activity may have therapeutic potential for the treatment of squamous carcinomas.

L7 ANSWER 8 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1075593 CAPLUS
DOCUMENT NUMBER: 143:352857
TITLE: Cosmetic compositions comprising an HDAC inhibitor in combination with a retinoid
INVENTOR(S): Schehlmann, Volker; Klock, Jochen; Maillan, Philippe Emmanuel; Vollhardt, Juergen H.; Rawlings, Anthony; Beumer, Raphael
PATENT ASSIGNEE(S): Dsm Ip Assets B.V., Neth.; Schehlmann, Volker; Klock, Jochen; Maillan, Philippe Emmanuel; Vollhardt, Juergen H.; Rawlings, Anthony; Beumer, Raphael
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092283	A1	20051006	WO 2005-EP3115	20050323 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1727516	A1	20061206	EP 2005-732360		20050323
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR					
CN 1933802	A	20070321	CN 2005-80009488		20050323
JP 2007530487	T	20071101	JP 2007-504354		20050323
IN 2006DN05303	A	20070803	IN 2006-DN5303		20060913
KR 2007012380	A	20070125	KR 2006-719817		20060925
US 20080227868	A1	20080918	US 2006-593487		20061031
PRIORITY APPLN. INFO.:			EP 2004-7281	A	20040326
			WO 2005-EP3115	W	20050323

OTHER SOURCE(S): MARPAT 143:352857

AB The present invention is directed to compns. which contain a combination of at least a histone deacetylase (HDAC) inhibitor, e.g., a phenylalkylcarboxylic acid, and a retinoid. The composition is in particular a cosmetic preparation It was found that the combination of an HDAC inhibitor and retinol or a derivative thereof is in particular useful for treating wrinkles but also for thickening the epidermis and for improving hair growth. Thus, an antiaging formulation contained retinol 0.50, and phenylbutyric acid 0.30%, in addition to the conventional cosmetic excipients.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1050682 CAPLUS
DOCUMENT NUMBER: 143:344601
TITLE: Gene expression profiles for diagnosing ovarian endometriosis
INVENTOR(S): Nakamura, Yusuke; Katagiri, Toyomasa
PATENT ASSIGNEE(S): Oncotherapy Science, Inc., Japan; The University of Tokyo
SOURCE: U.S. Pat. Appl. Publ., 52 pp., Cont.-in-part of Appl. No. PCT/JP04/013718.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050214836	A1	20050929	US 2005-69673	20050228 <--
WO 2004024952	A1	20040325	WO 2003-JP10257	20030812 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1932926 A2 20080618 EP 2008-152833 20030812

EP 1932926 A3 20081008

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR

WO 2005029089 A2 20050331 WO 2004-JP13718 20040914 <--

WO 2005029089 A3 20050602

WO 2005029089 A9 20060504

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2002-407365P P 20020830
US 2003-450920P P 20030228
WO 2003-JP10257 A2 20030812
US 2003-505572P P 20030924
WO 2004-JP13718 A2 20040914
EP 2003-795220 A3 20030812

AB Disclosed are methods of diagnosing ovarian endometriosis using 242 differentially expressed genes. Ovarian endometriosis-associated genes identified herein or their gene products are useful as a diagnostic markers for identifying or detecting ovarian endometriosis. Also disclosed are methods of screening compds. serving as agents for treating ovarian endometriosis, and methods of treating ovarian endometriosis and method or vaccinating a subject against ovarian endometriosis.

L7 ANSWER 10 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:902703 CAPLUS

DOCUMENT NUMBER: 143:272498

TITLE: Gene expression profiles in the diagnosis and treatment of Alzheimer's disease

INVENTOR(S): Landfield, Philip W.; Porter, Nada M.; Chen, Kuey Chu; Geddes, James; Blalock, Eric

PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA

SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005076939	A2	20050825	WO 2005-US3668	20050209 <--
WO 2005076939	A3	20060706		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 20070082350 A1 20070412 US 2006-501226 20060809
PRIORITY APPLN. INFO.: US 2004-542281P P 20040209
WO 2005-US3668 A 20050209

AB Genes showing altered patterns of expression in the brain that are associated with the neurol. changes found in Alzheimer's disease and that can be used in the early diagnosis of the disease, including the incipient form of the disease, are identified. The methods and kits of the invention utilize a set of genes and their encoded proteins that are shown to be correlated with incipient Alzheimer's disease.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:416465 CAPLUS
DOCUMENT NUMBER: 143:53809
TITLE: The book of opposites: The role of the nuclear receptor Co-regulators in the suppression of epidermal genes by retinoic acid and thyroid hormone receptors
AUTHOR(S): Jho, Sang H.; Vouthounis, Constantinos; Lee, Brian; Stojadinovic, Olivera; Im, Mark J.; Brem, Harold; Merchant, Ankit; Chau, Katherine; Tomic-Canic, Marjana
CORPORATE SOURCE: The Ronald O. Perelman Department of Dermatology, New York University School of Medicine, New York, NY, USA
SOURCE: Journal of Investigative Dermatology (2005), 124(5), 1034-1043
CODEN: JIDEAE; ISSN: 0022-202X
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Transcriptional regulation by nuclear receptors occurs through complex interactions that involve DNA response elements, co-activators/co-repressors, and histone modifying enzymes. Very little is known about how mol. interplay of these components may determine tissue specificity of hormone action. The authors have shown previously that retinoic acid (RA) and thyroid hormone (T3) repress transcription of a specific group of epidermal keratin genes through a novel mechanism that utilizes receptors homodimers. In this paper, the authors have analyzed the epidermal specificity of RA/T3 action by testing the role of co-repressors and co-activators in regulation of epidermal genes. Using transient co-transfections, northern blots, antisense oligonucleotides, and a histone deacetylase (HDAC) inhibitor, trichostatin A, the authors found that in the context of specific keratin RE (KRE), co-activators and histone acetylase become co-repressors of the RA/T3 receptors in the presence of their resp. ligands. Conversely, co-repressors and HDAC become co-activators of unliganded T3Rα. The receptor-co-activator interaction is intact and occurs through the NR-box. Therefore, the role of co-activator is to associate with liganded receptors, whereas the KRE-receptor interaction dets. specific transcriptional signal, in this case repression. This novel mol. mechanism of transcriptional repression conveys how RA and T3 target specific groups of epidermal genes, thus exerting intrinsic tissue specificity.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:394682 CAPLUS
DOCUMENT NUMBER: 142:445550
TITLE: Gene expression profiles for the diagnosis and prognosis of breast cancer
INVENTOR(S): Erlander, Mark; Ma, Xiao-Jun; Wang, Wei; Wittliff, James L.
PATENT ASSIGNEE(S): Arcturus Bioscience, Inc. University of Louisville, USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050095607	A1	20050505	US 2004-795092	20040305 <--
WO 2005098037	A1	20051020	WO 2004-US6760	20040305 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1651772	A1	20060503	EP 2004-718019	20040305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
JP 2007516692	T	20070628	JP 2006-532313	20040305

PRIORITY APPLN. INFO.: US 2003-453006P P 20030307
WO 2004-US6760 W 20040305

AB The invention relates to the identification and use of gene expression profiles, or patterns, suitable for identification of breast cancer patient populations with different survival outcomes. The gene expression profiles may be embodied in nucleic acid expression, protein expression, or other expression formats, and may be used in the study and/or determination of the prognosis of a patient, including breast cancer survival.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L7 ANSWER 13 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:315642 CAPLUS
DOCUMENT NUMBER: 142:353385
TITLE: Differentially expressed genes in human breast cancer and their diagnostic and therapeutic uses
INVENTOR(S): Munnes, Marc; Bojar, Hans
PATENT ASSIGNEE(S): Bayer Healthcare Ag, Germany
SOURCE: Eur. Pat. Appl., 542 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1522594	A2	20050413	EP 2004-15374	20040630 <--
EP 1522594	A3	20050622		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
EP 1892306	A2	20080227	EP 2007-22919	20040630
EP 1892306	A3	20080611		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
AU 2004283225	A1	20050506	AU 2004-283225	20041002 <--
CA 2530057	A1	20050506	CA 2004-2530057	20041002 <--
WO 2005040414	A1	20050506	WO 2004-EP11009	20041002 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1673471	A1	20060628	EP 2004-765764	20041002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007512804	T	20070524	JP 2006-530075	20041002
US 20090098533	A1	20090416	US 2006-561485	20060828
PRIORITY APPLN. INFO.:			EP 2003-22587 A	20031006
			EP 2004-15374 A3	20040630
			WO 2004-EP11009 W	20041002

AB The invention provides novel compns., methods and uses, for the prediction, diagnosis, prognosis, prevention and treatment of malignant neoplasia and breast cancer. The invention further relates to 185 genes that are differentially expressed in breast tissue of breast cancer patients vs. those of normal "healthy" tissue. Differentially expressed genes for the identification of patients which are likely to respond to chemotherapy are also provided.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:158474 CAPLUS

DOCUMENT NUMBER: 142:254569

TITLE: Derivatives of cyclic quinone that regulate gene expression for use in prevention or therapy of human diseases

INVENTOR(S): Padia, Janak K.; O'Brien, Sean; Lu, Jiemin; Pikul, Stanislaw

PATENT ASSIGNEE(S): Avalon Pharmaceuticals, USA

SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005016000	A1	20050224	WO 2004-US25038	20040803 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2003-492653P P 20030805
OTHER SOURCE(S): MARPAT 142:254569

AB This invention relates to production of cyclic quinone derivs. for use in regulation of gene expression, as relates to prevention or therapy of human diseases. Cyclic quinone synthesis schemes and structures are presented. With the goal of transcription regulation in diseased tissues, gene expression profile data is provided. The intended disease target for this invention is adenocarcinoma of the colon, however the invention claims application in numerous human diseases. Applications of the invention include production of cyclic quinone-based active ingredients in therapeutic agents.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:121193 CAPLUS
DOCUMENT NUMBER: 142:214836
TITLE: Biomarkers of cyclin-dependent kinase modulation in cancer therapy
INVENTOR(S): Li, Martha; Rupnow, Brent A.; Webster, Kevin R.; Jackson, Donald G.; Wong, Tai W.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012875	A2	20050210	WO 2004-US24424	20040729 <--
WO 2005012875	A3	20070315		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004262369	A1	20050210	AU 2004-262369	20040729 <--
CA 2533803	A1	20050210	CA 2004-2533803	20040729 <--
EP 1656542	A2	20060517	EP 2004-779471	20040729

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

JP 2007507204	T	20070329	JP 2006-522045		20040729
US 20070105114	A1	20070510	US 2006-567867		20060818
PRIORITY APPLN. INFO.:			US 2003-490890P	P	20030729
			WO 2004-US24424	W	20040729

AB Biomarkers having expression patterns that correlate with a response of cells to treatment with one or more cdk modulating agents, and uses thereof. Transcription profiling was used to identify the biomarkers. Specifically, transcription profiling of the effect of a certain cdk2 inhibitor (BMS 387032 0.5 L-tartaric acid salt) on peripheral blood mononuclear cells was first performed. Gene chips were used to quantitate the levels of gene expression on a large-scale with Affymetrix human gene chips HG-U95A, B, and C. Next, profiling of a cdk2 inhibitor-treated tumor cell line A28780 at multiple doses and time points was performed to establish a correlation of tumor site response with peripheral blood biomarkers. In order to establish the mol. target-specificity of the potential biomarkers, tumor cell line A2780 treated with anti-cdk2 oligonucleotides was also profiles. Overlapping gene expression changes were selected for further evaluation in human ovarian carcinoma xenograft A2780 that were treated with the cdk2 inhibitor. The selected biomarkers were subjected to real-time PCR anal. in order to verify the observed changes from the gene chip anal. The biomarker comprising GenBank accession number W28729 was discovered to have the most consistent and robust regulation in response to cdk inhibition. Provided are methods for testing or predicting whether a mammal will respond therapeutically to a method of treating cancer that comprises administering an agent that modulates cdk activity.

OS.CITING REF COUNT:	4	THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT:	3	THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	2005:99470 CAPLUS
DOCUMENT NUMBER:	142:197889
TITLE:	Fluoro substituted omega-carboxyaryl diphenyl urea for treatment of raf, VEGFR, PDGFR, p38 and flt-3 kinase-mediated diseases
INVENTOR(S):	Dumas, Jacques; Boyer, Stephen; Riedl, Bernd; Wilhelm, Scott
PATENT ASSIGNEE(S):	Bayer Pharmaceuticals Corporation, USA
SOURCE:	PCT Int. Appl., 68 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009961	A2	20050203	WO 2004-US23500	20040722 <--
WO 2005009961	A3	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

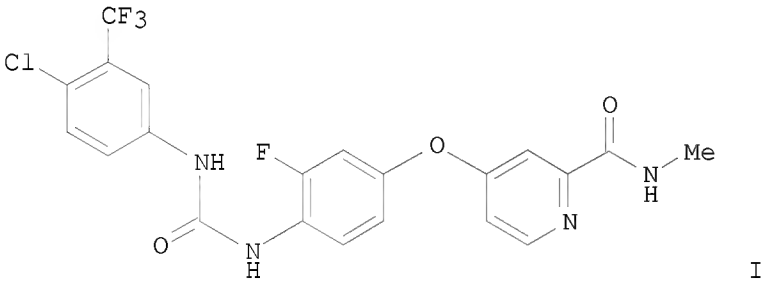
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004259760	A1	20050203	AU 2004-259760		20040722 <--
CA 2532865	A1	20050203	CA 2004-2532865		20040722 <--
US 20050038080	A1	20050217	US 2004-895985		20040722 <--
EP 1663978	A2	20060607	EP 2004-786091		20040722
EP 1663978	B1	20071128			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
BR 2004012219	A	20060822	BR 2004-12219		20040722
CN 1856469	A	20061101	CN 2004-80021091		20040722
JP 2006528196	T	20061214	JP 2006-521221		20040722
ES 2297490	T3	20080501	ES 2004-786091		20040722
ZA 2006000609	A	20070530	ZA 2006-609		20060120
KR 2006052866	A	20060519	KR 2006-701558		20060123
MX 2006000860	A	20060720	MX 2006-860		20060123
IN 2006DN00402	A	20070824	IN 2006-DN402		20060123
NO 2006000870	A	20060407	NO 2006-870		20060222
PRIORITY APPLN. INFO.:			US 2003-489102P	P	20030723
			US 2004-540326P	P	20040202
			WO 2004-US23500	W	20040722

OTHER SOURCE(S): CASREACT 142:197889

GI



I

AB Title compound I is prepared I and salts thereof is prepared in several steps from 3-fluoro-4-nitrophenol, 4-chloro-N-methylpyridine-2-carboxamide and 4-chloro-3-(trifluoromethyl)phenylisocyanate. I inhibits PDGFR tyrosine kinase with IC50 = 83 nM. I is useful for the treatment of, e.g., inflammation and as an antiproliferative agent.

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:71066 CAPLUS

DOCUMENT NUMBER: 142:170050

TITLE: DEF domain-containing members of the MAP kinase pathway and their use in screening for drug inhibitors

INVENTOR(S): Blenis, John; Murphy, Leon O.

PATENT ASSIGNEE(S): Harvard College, USA

SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005007090	A2	20050127	WO 2004-US21514	20040702 <--
WO 2005007090	A3	20090409		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2003-484761P P 20030703

AB Mitogen-activated protein (MAP) kinases (e.g., ERK1/2) phosphorylate a variety of target proteins including, for example, several immediate-early gene products (e.g., Fos, Myc, and Jun family proteins). Certain phosphorylation reactions require binding of the MAP kinase to the DEF domain of the target protein. Inhibitors that block this interaction may be useful therapeutics for human disease, including as antineoplastic agents. This invention provides several advantages over known therapies that directly target the MAP kinase signaling cascade. Typically, most compds. that inhibit the MAP kinase pathway are non-specific and inhibit more than one enzyme, and the targeted inhibited kinases are not available to perform normal physiol. functions necessary for cell survival, whereas therapeutic methods of the present invention inhibit the activation of particular target proteins and leave the MAP kinases enzymically active and available to phosphorylate other non-DEF domain-containing proteins. Thus, DEF domains are identified in a large number of proteins, and the principles of the invention are exemplified using the immediate-early gene, c-Fos. Screening assays useful for identifying compds. that inhibit the MAP kinase-DEF domain interaction are also disclosed.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L7 ANSWER 18 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:66610 CAPLUS
DOCUMENT NUMBER: 142:368954
TITLE: Identification of novel TCDD-regulated genes by microarray analysis
AUTHOR(S): Hanlon, Paul R.; Zheng, Wenchao; Ko, Alex Y.; Jefcoate, Colin R.
CORPORATE SOURCE: Molecular and Environmental Toxicology Center, University of Wisconsin-Madison, WI, 53706, USA
SOURCE: Toxicology and Applied Pharmacology (2005), 202(3), 215-228
CODEN: TXAPA9; ISSN: 0041-008X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB TCDD exposure of multipotential C3H10T1/2 fibroblasts for 72 h altered the expression of over 1000 genes, including coordinated changes across large functionally similar gene clusters. TCDD coordinately induced 23 cell cycle-related genes similar to epidermal growth factor (EGF)-induced levels but without any affect on the major mitogenic signaling pathway (extracellular signal-regulated kinase, ERK). TCDD treatment also decreased glycolytic and ribosomal clusters. Most of these TCDD-induced changes were attenuated by the presence of EGF or an

adipogenic stimulus, each added during the final 24 h. TCDD prevented 10% of EGF-induced gene responses and 40% of adipogenic responses. Over 100 other genes responded to TCDD during adipogenesis. This group of responses included complete suppression of three proliferins and stimulations of several cytokine receptors. Despite these varied secondary effects of TCDD, direct AhR activation measured by integrated AhR-responsive luciferase reporters was similar under quiescent, EGF-stimulated or adipogenic conditions. Only 23 genes were similarly induced by TCDD regardless of conditions and 10 were suppressed. These 23 genes include: 4 genes previously recognized to contain AhR response elements (cytochrome P 450 (CYP) 1B1, CYP1A1, NAD(P)H quinone reductase 1 (NQO1), and aldehyde dehydrogenase 3A1); two novel oxidative genes (alc. dehydrogenase 3 and superoxide dismutase 3); and glypican 1, a plasma membrane proteoglycan that affects cell signaling. Further expts. demonstrated that TCDD maximally induced NQO1, glypican 1 and alc. dehydrogenase 3 by 6 h. Glypican 1 activates the actions of many growth factors and therefore may contribute to secondary effects on gene expression.

OS.CITING REF COUNT: 29 THERE ARE 29 CAPLUS RECORDS THAT CITE THIS RECORD (29 CITINGS)

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:60754 CAPLUS
Correction of: 2004:1036571

DOCUMENT NUMBER: 142:233342
Correction of: 142:16836

TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy

INVENTOR(S): Liew, Choong-Chin

PATENT ASSIGNEE(S): Chondrogene Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 20040241727	A1	20041202	US 2004-812731	20040330	<--
US 20040014059	A1	20040122	US 2002-268730	20021009	<--
US 7598031	B2	20091006			
US 20070031841	A1	20070208	US 2003-601518	20030620	
US 20060134635	A1	20060622	US 2004-802875	20040312	
US 20050191637	A1	20050901	US 2004-803737	20040318	<--
US 20050196762	A1	20050908	US 2004-803759	20040318	<--
US 20050196763	A1	20050908	US 2004-803857	20040318	<--
US 20050196764	A1	20050908	US 2004-803858	20040318	<--
US 20050208505	A1	20050922	US 2004-803648	20040318	<--
US 20050208519	A1	20050922	US 2004-989191	20041115	<--
US 20090098564	A1	20090416	US 2008-287629	20081010	

PRIORITY APPLN. INFO.:

US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2001-271955P	P	20010228
US 2001-275017P	P	20010312
US 2001-305340P	P	20010713

	US 2002-85783	A2 20020228
	US 2004-812731	A2 20040330
	WO 2004-US20836	A2 20040621
	US 2004-989191	A3 20041115

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L7 ANSWER 20 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:34707 CAPLUS
DOCUMENT NUMBER: 142:128580
TITLE: Prognosis determination in Ewing sarcoma patients by genetic profiling
INVENTOR(S): Avigad, Smadar; Yaniv, Isaac; Zaizov, Rina; Ohali, Anat
PATENT ASSIGNEE(S): Mor Research Applications Ltd., Israel
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005002414	A2	20050113	WO 2004-IL578	20040630 <--
WO 2005002414	A3	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1641940	A2	20060405	EP 2004-744918	20040630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 20090227464	A1	20090910	US 2007-562527	20070423

PRIORITY APPLN. INFO.:	US 2003-483626P	P	20030701
	WO 2004-IL578	W	20040630

AB The present invention provides a method for assessing the prognosis of Ewing's sarcoma (ES) patients comprising determining the expression pattern of a defined set of genes in tumor material obtained from said patients, and assigning said expression pattern to either a good prognosis or poor prognosis group. It is possible to distinguish between ES patients having a good prognosis and those having a poor prognosis by comparing gene expression patterns in nucleic acid material isolated from the tumors. Furthermore, this prognosis determination may be performed very early on, during

initial diagnosis. Human Genome U95Av2 GeneChip microarrays (Affymetrix) were used to identify 818 genes differentially expressed in either the high-risk or the low-risk groups of 14 tumor samples, 7 tumors from patients who had progressed between 5 mo up to 5 years from diagnosis (defined as high-risk) and 7 tumors from patients who were disease-free for a low period of follow-up (defined as low-risk).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:1127487 CAPLUS

DOCUMENT NUMBER: 142:72870

TITLE: Gene expression profiles in airway epithelium and their use as signatures for diagnosing disorders of the lung

INVENTOR(S): Brody, Jerome S.; Spira, Avrum; Shah, Nila; Palma, John F.

PATENT ASSIGNEE(S): Trustees of Boston University, USA; Affymetrix, Inc.

SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111197	A2	20041223	WO 2004-US18492	20040610 <--
WO 2004111197	A3	20060720		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-477218P	P	20030610
US 2003-483387P	P	20030627
US 2003-497599P	P	20030825

AB A minimally invasive sample procurement method for obtaining airway epithelial cell RNA that can be analyzed by expression profiling, e.g., by array-based gene expression profiling, is disclosed. These methods can be used to identify patterns of gene expression that are diagnostic of lung disorders, e.g., cancer, to identify subjects at risk for developing lung disorders and to custom design an array, e.g., a microarray, for the diagnosis or prediction of lung disorders or susceptibility to lung disorders. Arrays and informative genes are also disclosed for this purpose.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:1081068 CAPLUS

DOCUMENT NUMBER: 142:51881

TITLE: Systems, methods and kits for characterizing phosphoproteomes by digestion, chromatography and mass spectrometry
INVENTOR(S): Gygi, Steven P.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108948	A2	20041216	WO 2004-US17613	20040604 <--
WO 2004108948	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20050164324	A1	20050728	US 2004-862195	20040604 <--

PRIORITY APPLN. INFO.: US 2003-476010P P 20030604

AB The invention provides systems, software, methods and kits for detecting and/or quantifying phosphorylatable polypeptides and/or acetylated polypeptides in complex mixts., such as a lysate of a cell or cellular compartment (e.g., such as an organelle). The methods can be used in high throughput assays to profile phosphoproteomes and to correlate sites and amts. of phosphorylation with particular cell states.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1033549 CAPLUS
DOCUMENT NUMBER: 142:758
TITLE: Methods and compositions using immunomodulatory compounds for treatment and management of cancers and other angiogenesis-associated diseases
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103274	A2	20041202	WO 2004-US14004	20040505 <--
WO 2004103274	A3	20050303		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 20040029832	A1	20040212	US 2003-438213	20030515	<--
CA 2505128	A1	20040527	CA 2003-2505128	20031106	<--
CA 2505128	C	20080916			
AU 2003290651	A1	20040603	AU 2003-290651	20031106	<--
AU 2003290651	B2	20080131			
EP 1567158	A2	20050831	EP 2003-783233	20031106	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003016050	A	20050913	BR 2003-16050	20031106	<--
JP 2006514689	T	20060511	JP 2005-507108	20031106	
US 20060199843	A1	20060907	US 2003-704237	20031106	
US 7323479	B2	20080129			
NZ 540385	A	20090131	NZ 2003-540385	20031106	
AU 2004240548	A1	20041202	AU 2004-240548	20040505	<--
CA 2525557	A1	20041202	CA 2004-2525557	20040505	<--
EP 1635826	A2	20060322	EP 2004-751400	20040505	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR					
BR 2004010306	A	20060523	BR 2004-10306	20040505	
CN 1822834	A	20060823	CN 2004-80020445	20040505	
JP 2006528973	T	20061228	JP 2006-532787	20040505	
ZA 2005009232	A	20070328	ZA 2005-9232	20040505	
RU 2348407	C2	20090310	RU 2005-139133	20040505	
MX 2005004734	A	20050802	MX 2005-4734	20050503	<--
MX 2005012155	A	20060222	MX 2005-12155	20051111	
IN 2005CN03418	A	20070727	IN 2005-CN3418	20051215	
AU 2006202316	A1	20060622	AU 2006-202316	20060531	
AU 2006202316	B2	20080410			
US 20080132541	A1	20080605	US 2007-557302	20070906	
US 20080138295	A1	20080612	US 2008-69473	20080211	
AU 2008201343	A1	20080424	AU 2008-201343	20080320	
IN 2008CN05127	A	20090320	IN 2008-CN5127	20080925	

PRIORITY APPLN. INFO.:	US 2003-438213	A	20030515
	US 2003-704237	A	20031106
	US 2002-380842P	P	20020517
	US 2002-424600P	P	20021106
	AU 2003-234626	A3	20030516
	WO 2003-US35544	W	20031106
	WO 2004-US14004	W	20040505
	US 2005-534325	A3	20050912
	IN 2005-CN3418	A3	20051215
	AU 2006-202316	A3	20060531

OTHER SOURCE(S): MARPAT 142:758

AB Methods are disclosed for treating, preventing and/or managing cancer, as well as and diseases and disorders associated with, or characterized by, undesired angiogenesis. Specific methods encompass the administration of an immunomodulatory compound alone or in combination with a second active ingredient. The invention further discloses methods for reducing or avoiding adverse side effects associated with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy, which comprise the administration of an immunomodulatory compound Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:965067 CAPLUS
DOCUMENT NUMBER: 141:406039
TITLE: Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis
INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A.
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424 <--
WO 2004096224	A3	20041216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1473043	A1	20041103	EP 2003-9587	20030429 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004233576	A1	20041111	AU 2004-233576	20040424 <--
CA 2523868	A1	20041111	CA 2004-2523868	20040424 <--
EP 1622619	A2	20060208	EP 2004-729366	20040424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004009919	A	20060425	BR 2004-9919	20040424
JP 2006524634	T	20061102	JP 2006-500099	20040424
IN 2005DN04018	A	20091002	IN 2005-DN4018	20050907
MX 2005011656	A	20051215	MX 2005-11656	20051028 <--
NO 2005005605	A	20051128	NO 2005-5605	20051128 <--

PRIORITY APPLN. INFO.:		
EP 2003-9587	A	20030429
EP 2004-508	A	20040113
EP 2004-1171	A	20040121
WO 2004-EP4363	W	20040424

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic

or naturally occurring semisynthetic or synthetic agents.

OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 25 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:515678 CAPLUS

DOCUMENT NUMBER: 141:48625

TITLE: Characterization of regulatory regions of genes by the effect of chromatin modifying agents on DNase I hypersensitivity and mapping of labile regions

INVENTOR(S): Stamatoyannopoulos, John A.; McArthur, Michael; Dorschner, Michael O.; Hawrylycz, Michael; Humbert, Rich; Stamatoyannopoulos, George; Alden, Rhett; Clendenning, James

PATENT ASSIGNEE(S): Regulome Corporation, USA

SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004053106	A2	20040624	WO 2003-US40070		20031205 <--
WO 2004053106	A3	20060908			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003302777	A1	20040630	AU 2003-302777		20031205 <--
PRIORITY APPLN. INFO.:			US 2002-431597P	P	20021205
			US 2003-492171P	P	20030801
			WO 2003-US40070	W	20031205

AB The invention provides methods for quant. profiling of chromatin sensitivity to a DNA modifying agent. Regulatory regions associated with sites that can be induced to be DNase I hypersensitive can be characterized by anal. of overlapping regions covering the site to determine the chromatin architecture of the region. Regulatory site profiles associated with specific genes are particularly useful for discovery of medicinal agents, other genomic sequences involved in gene regulation, and regulatory mechanisms that are involved in health and disease. The regulatory sequence profiles also are highly valuable when used by computer programs for comparing known and unknown genetic sequences by a large variety of exptl. and computer manipulations. The methods involve identifying a DNase I hypersensitive site and then analyzing the hypersensitivity in greater detail using a series of overlapping sequences to cover the local chromatin region. Cleavage by DNase I is assayed by PCR, with labile sites no longer being amplifiable.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 26 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:737878 CAPLUS
DOCUMENT NUMBER: 139:256234
TITLE: Methods for detecting epigenetically silenced tumor suppressor genes and uses in human cancer diagnosis and therapy
INVENTOR(S): Sidransky, David
PATENT ASSIGNEE(S): The Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076594	A2	20030918	WO 2003-US7245	20030307 <--
WO 2003076594	A3	20070518		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA				
CA 2478510	A1	20030918	CA 2003-2478510	20030307 <--
AU 2003230616	A1	20030922	AU 2003-230616	20030307 <--
US 20040081976	A1	20040429	US 2003-383864	20030307 <--
EP 1578924	A2	20050928	EP 2003-723702	20030307 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005532041	T	20051027	JP 2003-574801	20030307 <--
CN 101080499	A	20071128	CN 2003-809647	20030307
PRIORITY APPLN. INFO.:			US 2002-362577P P	20020307
			WO 2003-US7245 W	20030307

AB Methods of genomic screening to detect epigenetically silenced genes associated with cancer, including epigenetically silenced tumor suppressor genes, are provided. Also provided are methods of detecting a cancer, for example, an esophageal squamous cell carcinoma or a head and neck squamous cell carcinoma, and methods of treating a subject having such a cancer. Microarrays were used to identify potential epigenetically silenced tumor suppressor genes whose expression was upregulated following treatment with a demethylating agent and/or histone deacetylase inhibitor. A number of genes, downregulated in human esophageal cancer and head and neck cancer cells, were shown to contain heavy cytosine methylation in CpG sites and CpG islands in their promoter regions. The roles of these genes in carcinogenesis is discussed and their use for cancer therapy is disclosed.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L7 ANSWER 27 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:662654 CAPLUS
DOCUMENT NUMBER: 139:301507
TITLE: Identification and Characterization of a Cell Cycle and Apoptosis Regulatory Protein-1 as a Novel Mediator of Apoptosis Signaling by Retinoid CD437

AUTHOR(S): Rishi, Arun K.; Zhang, Liyue; Boyanapalli, Madanamohan; Wali, Anil; Mohammad, Ramzi M.; Yu, Yingjie; Fontana, Joseph A.; Hatfield, James S.; Dawson, Marcia I.; Majumdar, Adhip P. N.; Reichert, Uwe

CORPORATE SOURCE: Department of Internal Medicine and Karmanos Cancer Institute, Veterans Affairs Medical Center, Wayne State University, Detroit, MI, 48201, USA

SOURCE: Journal of Biological Chemistry (2003), 278(35), 33422-33435
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB CD437, a novel retinoid, causes cell cycle arrest and apoptosis in a number of cancer cells including human breast carcinoma (HBC) by utilizing an undefined retinoic acid receptor/retinoid X receptor-independent mechanism. To delineate mediators of CD437 signaling, we utilized a random antisense-dependent functional knockout genetic approach. We identified a cDNA that encodes .apprx.130-kDa HBC cell perinuclear protein (termed CARP-1). Treatments with CD437 or chemotherapeutic agent adriamycin, as well as serum deprivation of HBC cells, stimulate CARP-1 expression. Reduced levels of CARP-1 result in inhibition of apoptosis by CD437 or adriamycin, whereas increased expression of CARP-1 causes elevated levels of cyclin-dependent kinase inhibitor p21WAF1/CIP1 and apoptosis. CARP-1 interacts with 14-3-3 protein as well as causes reduced expression of cell cycle regulatory genes including c-Myc and cyclin B1. Loss of c-Myc sensitizes cells to apoptosis by CARP-1, whereas expression of c-Myc or 14-3-3 inhibits CARP-1-dependent apoptosis. Thus, apoptosis induction by CARP-1 involves sequestration of 14-3-3 and CARP-1-mediated altered expression of multiple cell cycle regulatory genes. Identification of CARP-1 as a key mediator of signaling by CD437 or adriamycin allows for delineation of pathways that, in turn, may prove beneficial for design and targeting of novel antitumor agents.

OS.CITING REF COUNT: 26 THERE ARE 26 CAPLUS RECORDS THAT CITE THIS RECORD (26 CITINGS)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 28 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:492204 CAPLUS

DOCUMENT NUMBER: 139:64331

TITLE: Modular biochip arrays and their diagnostic or analytical uses and their preparation and uses

INVENTOR(S): Bignon, Yves Jean; Vidal, Veronique; D'Incan, Chantal; Laplace, Chambaud Valerie; Sylvain, Vidal Valerie

PATENT ASSIGNEE(S): Centre Medico Chirurgical De Tronquieres, Fr.

SOURCE: Fr. Demande, 124 pp.
CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2833968	A1	20030627	FR 2001-16962	20011220 <--

PRIORITY APPLN. INFO.: FR 2001-16962 20011220

AB A method of constructing microarrays for specific diagnostic or research purposes is described. The microarrays are made up of modular sections

with each module containing probes for a defined set of genes that can be assembled to give an array suitable for a specific purposes. The individual modules may be on sep. supports.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 29 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:294123 CAPLUS

DOCUMENT NUMBER: 139:50814

TITLE: Repression of E2F1-mediated transcription by the ErbB3 binding protein Ebp1 involves histone deacetylases

AUTHOR(S): Zhang, Yuexing; Woodford, Nicholas; Xia, Xianmin; Hamburger, Anne W.

CORPORATE SOURCE: Greenebaum Cancer Center, Univ. Maryland, Baltimore, MD, USA

SOURCE: Nucleic Acids Research (2003), 31(8), 2168-2177
CODEN: NARHAD; ISSN: 0305-1048

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ebp1, an ErbB3 binding protein that is a member of the proliferation-associated PA2G4 family, inhibits the proliferation and induces the differentiation of human ErbB pos. breast and prostate cancer cell lines. Ebp1 binds the tumor suppressor retinoblastoma protein (Rb) both in vivo and in vitro, and Rb and Ebp1 cooperate to inhibit the transcription of the E2F1-regulated cyclin E promoter. We show here that Ebp1 can inhibit the transcription of other E2F-regulated reporter genes and of several endogenous E2F-regulated genes important in cell cycle progression in both Rb pos. and Rb null cells. The Ebp1-mediated transcriptional repression depended on the presence of an E2F1 consensus element in the promoters. A fusion of Ebp1 with the GAL4 DNA binding domain protein had independent transcriptional repression activity that mapped to the C-terminal region of Ebp1. This C-terminal region of Ebp1 bound functional histone deacetylase (HDAC) activity and inhibitors of HDAC significantly reduced Ebp1-mediated repression. Ebp1 bound HDAC2, but not HDAC1, in vitro. An Ebp1 mutant lacking the HDAC binding domain failed to inhibit transcription. Our results suggest that Ebp1 can repress transcription of some E2F-regulated promoters and that one mechanism of Ebp1- mediated transcriptional repression is via its ability to recruit HDAC activity.

OS.CITING REF COUNT: 31 THERE ARE 31 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 30 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:242177 CAPLUS

DOCUMENT NUMBER: 138:265692

TITLE: Retinoid receptor pan-antagonists for stimulating chondrogenesis

INVENTOR(S): Underhill, Tulley Michael; Weston, Andrea D.

PATENT ASSIGNEE(S): The University of Western Ontario, Can.

SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024473	A2	20030327	WO 2002-CA1421	20020917 <--
WO 2003024473	A3	20030807		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2459949	A1	20030327	CA 2002-2459949	20020917 <--
AU 2002325752	A1	20030401	AU 2002-325752	20020917 <--
EP 1427399	A2	20040616	EP 2002-760008	20020917 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

US 20050009868	A1	20050113	US 2004-489750	20040827 <--

PRIORITY APPLN. INFO.:	US 2001-322874P	P	20010917
	WO 2002-CA1421	W	20020917

AB The invention provides methods and compns. for inducing or enhancing chondrogenesis in vivo and/or ex vivo. More specifically, the invention discloses the use of RAR pan-antagonist compns. for the treatment, repair and engineering of cartilage.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 31 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:219666 CAPLUS

DOCUMENT NUMBER: 138:231716

TITLE: Valproic acid and derivatives thereof for the combination therapy of human cancers, for the treatment of tumor metastasis and minimal residual disease

INVENTOR(S): Heinzel, Thorsten; Gottlicher, Martin; Hentsch, Bernd; Wels, Winfried Stephan; Pelicci, Pier Giuseppe; Minucci, Saverio; Herrlich, Peter A.; Groner, Bernd

PATENT ASSIGNEE(S): G2M Cancer Drugs AG, Germany

SOURCE: Eur. Pat. Appl., 61 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1293205	A1	20030319	EP 2001-121722	20010918 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

CA 2460713	A1	20030327	CA 2002-2460713	20020917 <--
WO 2003024442	A2	20030327	WO 2002-EP10419	20020917 <--
WO 2003024442	A3	20030918		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002338716	A1	20030401	AU 2002-338716	20020917 <--
AU 2002338716	B2	20070816		
EP 1427403	A2	20040616	EP 2002-777129	20020917 <--
EP 1427403	B1	20051228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
EP 1529527	A2	20050511	EP 2005-101081	20020917 <--
EP 1529527	A3	20050525		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
JP 2005512961	T	20050512	JP 2003-528538	20020917 <--
EP 1602371	A2	20051207	EP 2005-19659	20020917 <--
EP 1602371	A3	20061115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
AT 314063	T	20060115	AT 2002-777129	20020917
ES 2252519	T3	20060516	ES 2002-777129	20020917
US 20050038113	A1	20050217	US 2004-489770	20041029 <--
AU 2007207869	A1	20070906	AU 2007-207869	20070816
AU 2007207869	B2	20090910		

PRIORITY APPLN. INFO.:	EP 2001-121722	A 20010918
	AU 2002-338716	A3 20020917
	EP 2002-777129	A3 20020917
	WO 2002-EP10419	W 20020917

OTHER SOURCE(S): MARPAT 138:231716

AB The invention discloses the use of valproic acid and derivs. thereof as inhibitors of enzymes having histone deacetylase activity for the therapeutic treatment of human cancers in combination with established therapeutic principles. The invention also discloses the use of these compds. for the treatment of tumor metastasis and minimal residual disease. The invention includes the manufacture of a clin. used substance for the treatment of human cancers.

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 32 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:69730 CAPLUS

DOCUMENT NUMBER: 139:30324

TITLE: Cell cycle blockade and differentiation of ovarian cancer cells by the histone deacetylase inhibitor trichostatin A are associated with changes in p21, Rb, and Id proteins

AUTHOR(S): Strait, Kevin A.; Dabbas, Bashar; Hammond, Elizabeth H.; Warnick, C. Terry; Ilstrup, Sarah J.; Ford, Clyde D.

CORPORATE SOURCE: Department of Medicine, Cancer Research Laboratory, LDS Hospital, Salt Lake City, UT, 84143, USA

SOURCE: Molecular Cancer Therapeutics (2002), 1(13), 1181-1190
CODEN: MCTOCF; ISSN: 1535-7163

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inhibitors of histone deacetylase activity are

emerging as a potentially important new class of anticancer agents. In the current studies, exposing A2780 ovarian cancer cells to the histone deacetylase inhibitor trichostatin A (TSA) produced a marked change in cellular morphol., proliferation, and differentiation. Within 24 h of TSA treatment, there was a morphol. transformation of the cells, with increased cytoplasm, a more epithelial-like columnar appearance, and the emergence of distinct cellular boundaries. Commensurate with the morphol. transformation, TSA also inhibited cell proliferation; cells treated with TSA for 72 h increased to 110% of the initial cell nos. vs. control cell nos. of 622%, with a corresponding reduction in mitotic activity and a flow cytometry S-phase fraction of 3.9% in TSA-treated cells vs. 28.8% for control. TSA also induced epithelial-like differentiation with increased cytokeratin expression from 2% of controls to 22-25% of TSA-treated cells and the reappearance of intercellular plasma membrane junctions and primitive microvilli. Immunocytochem. analyses indicate the mol. mechanism underlying the actions of TSA on A2780 cell cycle progression and differentiation involves reexpression of the CDK inhibitor p21. Elevated levels of p21, in TSA-treated cells, were associated with a reduction in the phosphorylation of the cell cycle regulator retinoblastoma protein (Rb). TSA also caused a decrease in the helix-loop-helix inhibitor of differentiation/DNA binding protein Id1, with no change in Id2 levels. In conclusion, the observed TSA-induced changes in p21, Rb, and Id1 are consistent with cell cycle senescence and differentiation of A2780 ovarian cancer cells.

OS.CITING REF COUNT: 42 THERE ARE 42 CAPLUS RECORDS THAT CITE THIS RECORD (42 CITINGS)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 33 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:937303 CAPLUS

DOCUMENT NUMBER: 138:20443

TITLE: Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes

INVENTOR(S): Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin

PATENT ASSIGNEE(S): Takara Bio Inc., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2002355079	A	20021210	JP 2002-69354		20020313 <--
PRIORITY APPLN. INFO.:			JP 2001-73183	A	20010314
			JP 2001-74993	A	20010315
			JP 2001-102519	A	20010330

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises preparing a nucleic acid sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate,

dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-β estradiol (E2), were found in mice by DNA chip anal.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

L7 ANSWER 34 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:521969 CAPLUS
DOCUMENT NUMBER: 137:90000
TITLE: Protein-protein interactions in adipocyte cells and method for selecting modulators of these interactions
INVENTOR(S): Legrain, Pierre; Marullo, Stefano; Jockers, Ralf
PATENT ASSIGNEE(S): Hybrigenics, Fr.; Centre National De La Recherche Scientifique
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053726	A2	20020711	WO 2001-EP15423	20011228 <--
WO 2002053726	A3	20030313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002240892	A1	20020716	AU 2002-240892	20011228 <--
US 20030040089	A1	20030227	US 2002-38010	20020102 <--
PRIORITY APPLN. INFO.:			US 2001-259377P P	20010102
			WO 2001-EP15423 W	20011228

AB The present invention relates to protein-protein interactions of adipocyte. More specifically, the present invention relates to complexes of polypeptides, or polynucleotides encoding the polypeptides, fragments of the polypeptides, antibodies to the complexes. Selected Interacting Domains (SID) which are identified due to the protein-protein interactions, methods for screening drugs for agents which modulate the interaction of proteins, and pharmaceutical compns. that are capable of modulating the protein-protein interactions are further disclosed.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 35 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:58582 CAPLUS
DOCUMENT NUMBER: 137:149858
TITLE: Down-stream regions of the POZ-domain influence the interaction of the t(11;17)-associated PLZF/RARα fusion protein with the histone-deacetylase recruiting co-repressor complex
AUTHOR(S): Puccetti, Elena; Sennewald, Birgit; Fosca-Ferrara, Fabiana; Boehrer, Simone; Bianchini, Andrea; Hoelzer, Dieter; Ottmann, Oliver Gerhard; Nervi, Clara; Ruthardt, Martin

CORPORATE SOURCE: Johann Wolfgang Goethe-Universitat, Frankfurt, D-60590, Germany
SOURCE: Hematology Journal (2001), 2(6), 385-392
CODEN: HJEOBZ; ISSN: 1466-4860
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Introduction: Acute promyelocytic leukemia (APL) patients with t(15;17)(PML/RARα pos.) achieve remission upon all-trans-retinoic acid (t-RA) treatment, whereas patients with t(11;17)(PLZF/RARα pos.) do not. Both APL translocation products bind to the histone deacetylase (HD)-recruiting nuclear co-repressor complex (HD-NCR) in a ligand-dependent manner through their RARα portion. Differently to PML/RARα, PLZF/RARα also binds the HD-NCR in a ligand-independent manner through the PLZF portion of the fusion protein (PLZF#), which seems to be crucial for the t-RA resistance of t(11;17) APL patients. Materials and methods: The t-RA sensitivity of U937 cells was tested by the nitro-blue tetrazolium reduction (NBT) assay and by anal. of t-RA-induced type II transglutaminase activity. The interaction between HD-NCR and PLZF/RARα was investigated by in vitro binding assays. Results: (i) Deletions in PLZF# convert PLZF/RARα from a repressor to an activator of t-RA response in U937 cells; (ii) the effect of PLZF/RARα on t-RA-signaling is regulated by the POZ-domain and its down-stream regions of PLZF#; (iii) there are addnl. binding sites for HD-NCR in PLZF# and (iv) PLZF# not only directly binds but also regulates the binding of PLZF/RARα to the HD-NCR. Conclusions: At least two different mechanisms responsible for the aberrant recruitment of HD-NCR complexes by PLZF# are regulating the different t-RA-sensitivity of the PLZF/RARα and PML/RARα pos. APL blasts: one is related to the direct binding of the different members of the HD-NCR complex to PLZF#; the other is an enforcing effect of PLZF# on the affinity of the PLZF/RARα fusion protein to the HD-NCR complex.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 36 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:890367 CAPLUS
DOCUMENT NUMBER: 137:72315
TITLE: ATRA in the treatment of acute promyelocytic leukemia
AUTHOR(S): Ozpolat, B.; Lopez-Berestein, G.; Mehta, K.
CORPORATE SOURCE: Department of Bioimmunotherapy, Section of Immunobiology and Drug Carriers MD Anderson Cancer Center, The University of Texas, Houston, TX, USA
SOURCE: Journal of Biological Regulators and Homeostatic Agents (2001), 15(2), 107-122
CODEN: JBRAER; ISSN: 0393-974X
PUBLISHER: Wichtig Editore
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Acute promyelocytic leukemia (APL) is a unique disease that responds to differentiation-inducing effects of all-trans-retinoic acid (ATRA). ATRA induces complete clin. remissions (CRs) in most patients and now constitutes a standard therapy in patients with APL. However, CRs induced by ATRA are usually brief, and resistance to the therapy rapidly develops, leading to relapses in almost every patient; thus limiting the use of ATRA as a single agent. On the basis of clin. and in vitro studies, the following mechanisms have been proposed to explain ATRA resistance: (1) induction of accelerated metabolism of ATRA, (2) increased expression of cellular retinoic acid-binding proteins

(CRABPs), (3) constitutive degradation of PML-RARα, (4) point mutations in the ligand-binding domain of RARα of PML-RARα, (5) P-glycoprotein expression, (6) transcriptional repression by histone deacetylase activity, (7) isoforms of PML-RARα, (8) persistent telomerase activity, and (9) expression of type II transglutaminase. In this review, we discuss the evidence provided in support of each mechanism, the mechanism's possible impact on the outcome of APL, and the newer approaches that are being employed to overcome ATRA resistance.

OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)

REFERENCE COUNT: 172 THERE ARE 172 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 37 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:775265 CAPLUS

DOCUMENT NUMBER: 136:132090

TITLE: Investigation of differentially expressed genes during the development of mouse cerebellum

AUTHOR(S): Kagami, Yoshihiro; Furuichi, Teiichi

CORPORATE SOURCE: Laboratory for Molecular Neurogenesis, Brain Science Institute, RIKEN, Wako, 351-0198, Japan

SOURCE: Gene Expression Patterns (2001), 1(1), 39-59
CODEN: GEPEAD; ISSN: 1567-133X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Before the discovery of DNA microarray and DNA chip technol., the expression of only a small number of genes could be analyzed at a time. Currently, such technol. allows us the simultaneous anal. of a large number of genes to systematically monitor their expression patterns that may be associated with various biol. phenomena. We utilized the Affymetrix GeneChip Mu11K to analyze the gene expression profile in developing mouse cerebellum to assist in the understanding of the genetic basis of cerebellar development in mice. Our anal. showed 81.6% (10.321/12.654) of the genes represented on the GeneChip were expressed in the postnatal cerebellum, and among those, 8.7% (897/10.321) were differentially expressed with more than a two-fold change in their maximum and min. expression levels during the developmental time course. Further anal. of the differentially expressed genes that were clustered in terms of their expression patterns and the function of their encoded products revealed an aspect of the genetic foundation that lies beneath the cellular events and neural network formation that takes place during the development of the mouse cerebellum.

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 38 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:525041 CAPLUS

DOCUMENT NUMBER: 135:255297

TITLE: Novel patterns of gene expression in pituitary adenomas identified by complementary deoxyribonucleic acid microarrays and quantitative reverse transcription-polymerase chain reaction

AUTHOR(S): Evans, Chheng-Orn; Young, Andrew N.; Brown, Milton R.; Brat, Daniel J.; Parks, John. S.; Neish, Andrew S.; Oyesiku, Nelson M.

CORPORATE SOURCE: Department of Neurosurgery and Laboratory of Molecular Neurosurgery and Biotechnology, Emory University

School of Medicine, Atlanta, GA, 30322, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism (2001), 86(7), 3097-3107
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pituitary adenomas account for approx. 10% of intracranial tumors, but little is known of the oncogenesis of these tumors. The identification of tumor-specific genes may further elucidate the pathways of tumor formation. We used complementary DNA microarrays to examine gene expression profiles in nonfunctioning, PRL, GH, and ACTH secreting adenomas, compared with normal pituitary. Microarray anal. showed that 128 of 7075 genes examined were differentially expressed. We then analyzed three genes with unique expression patterns and oncogenic importance by RT-real time quant. PCR in 37 pituitaries. Folate receptor gene was significantly overexpressed in nonfunctioning adenomas but was significantly underexpressed in PRL and GH adenomas, compared with controls and to other tumors. The ornithine decarboxylase gene was significantly overexpressed in GH adenomas, compared with other tumor subtypes but was significantly underexpressed in ACTH adenomas. C-mer proto-oncogene tyrosine kinase gene was significantly overexpressed in ACTH adenomas but was significantly underexpressed in PRL adenomas. We have shown that at least three genes involved in carcinogenesis in other tissues are also aberrantly regulated in the major types of pituitary tumors. The evaluation of candidate genes that emerge from these expts. provides a rational approach to investigate those genes significant in tumorigenesis.
OS.CITING REF COUNT: 57 THERE ARE 57 CAPLUS RECORDS THAT CITE THIS RECORD (57 CITINGS)
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 39 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:354388 CAPLUS
DOCUMENT NUMBER: 135:105661
TITLE: Growth and gene expression profile analyses of endometrial cancer cells expressing exogenous PTEN
AUTHOR(S): Matsushima-Nishiu, Mieko; Unoki, Motoko; Ono, Kenji; Tsunoda, Tatsuhiko; Minaguchi, Takeo; Kuramoto, Hiroyuki; Nishida, Masato; Satoh, Toyomi; Tanaka, Toshihiro; Nakamura, Yusuke
CORPORATE SOURCE: Laboratories of Molecular Medicine, Human Genome Center, Institute of Medical Science, The University of Tokyo, Tokyo, 108-8639, Japan
SOURCE: Cancer Research (2001), 61(9), 3741-3749
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The PTEN tumor suppressor gene encodes a multifunctional phosphatase that plays an important role in inhibiting the phosphatidylinositol-3-kinase pathway and downstream functions that include activation of Akt/protein kinase B, cell survival, and cell proliferation. Enforced expression of PTEN in various cancer cell lines decreases cell proliferation through arrest of the cell cycle, accompanied in some cases by induction of apoptosis. We used cDNA microarrays containing 4009 cDNAs to examine changes in gene-expression profiles when exogenous PTEN was induced in PTEN-defective cells. The microarrays and subsequent semiquant. reverse transcription-PCR anal. revealed transcriptional stimulation of 99 genes and repression of 72 genes. Some of the differentially expressed genes already had been implicated in cell proliferation, differentiation,

apoptosis, or cell cycle control, e.g., overexpression of PTEN-induced transactivation of cyclin-dependent inhibitor 1B (p27Kip1) and 2B (p15INK4B), members of the TNF receptor family, tumor necrosis factor-associated genes, and members of the Notch-signaling and Mad families. To our knowledge this is the first report of transactivation of those genes by PTEN. The genes differentially expressed in our expts. also included many whose correlation with cancer development had not been recognized before. Our data should contribute to a greater understanding of the broad spectrum of ways in which PTEN affects intracellular signaling pathways. Anal. of expression profiles with microarrays appears to be a powerful approach for identifying anticancer genes and/or disease-specific targets for cancer therapy.

OS.CITING REF COUNT: 41 THERE ARE 41 CAPLUS RECORDS THAT CITE THIS RECORD (42 CITINGS)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 40 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:338762 CAPLUS

DOCUMENT NUMBER: 134:362292

TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile

INVENTOR(S): Farr, Spencer

PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA

SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103 <--
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic

damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 41 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:168726 CAPLUS

DOCUMENT NUMBER: 135:150720

TITLE: A functionally active RARα nuclear receptor is expressed in retinoic acid non responsive early myeloblastic cell lines

AUTHOR(S): Grande, A.; Montanari, M.; Manfredini, R.; Tagliafico, E.; Zanocco-Marani, T.; Trevisan, F.; Ligabue, G.; Siena, M.; Ferrari, St; Ferrari, Se

CORPORATE SOURCE: Dipartimento di Scienze Biomediche, Sezione di Chimica Biologica, Universita di Modena e Reggio Emilia, Modena, 41100, Italy

SOURCE: Cell Death and Differentiation (2001), 8(1), 70-82
CODEN: CDDIEK; ISSN: 1350-9047

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Although all-trans retinoic acid (ATRA) can restore the differentiation capacity of leukemic promyelocytes, early leukemic myeloblasts are conversely not responsive to ATRA induced granulocytic differentiation. To assess whether this resistance to ATRA is related to an impaired function of the Retinoic Acid Receptor α (RARα), the authors performed an anal. of RARα expression and transactivation activity, in several myeloidleukemic cell lines, representative of different types of spontaneous acute myeloid leukemias. These results indicate that a functionally active RARα nuclear receptor is expressed in all the analyzed cell lines, regardless of their differentiation capacity following exposure to ATRA. The observation that ATRA treatment is able to induce the expression of retinoic acid target genes, in late- but not in early-myeloblastic leukemic cells, raises the possibility that the differentiation block of these cells is achieved through a chromatin mediated mechanism. Acetylation is apparently not involved in this process, since the histone deacetylase inhibitor trichostatin A, is not able to restore the differentiation capacity of early leukemic myeloblasts. Further investigation is needed to clarify whether myeloid transcription factors, distinct to RARα, play a role in the resistance of these cells to ATRA treatment.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

L7 ANSWER 42 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:64506 CAPLUS

DOCUMENT NUMBER: 137:91258

TITLE: ES cell neural differentiation reveals a substantial number of novel ESTs. [Erratum to document cited in CA135:150370]

AUTHOR(S): Bain, G.; Mansergh, F. C.; Wride, M. A.; Hance, J. E.; Isogawa, A.; Rancourt, S. L.; Ray, W. J.; Yoshimura, Y.; Tsuzuki, T.; Gottlieb, D. I.; Rancourt, D. E.

CORPORATE SOURCE: Department of OncologyDepartment of Biochemistry and Molecular Biology, The University of Calgary, Calgary, AB, T2N 4N1, Can.

SOURCE: Functional & Integrative Genomics (2000), 1(3), 218-219
CODEN: FIGUBY; ISSN: 1438-793X
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The captions for Figure 1 and Figure 2 were reversed.

L7 ANSWER 43 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:59749 CAPLUS
DOCUMENT NUMBER: 135:150370
TITLE: ES cell neural differentiation reveals a substantial number of novel ESTs
AUTHOR(S): Bain, G.; Mansergh, F. C.; Wride, M. A.; Hance, J. E.; Isogawa, A.; Rancourt, S. L.; Ray, W. J.; Yoshimura, Y.; Tsuzuki, T.; Gottlieb, D. I.; Rancourt, D. E.
CORPORATE SOURCE: Department of Oncology, Department of Biochemistry and Molecular Biology, The University of Calgary, Calgary, AB, T2N 4N1, Can.
SOURCE: Functional & Integrative Genomics (2000), 1(2), 127-139
CODEN: FIGUBY; ISSN: 1438-793X
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method was used for synchronously differentiating murine embryonic stem (ES) cells into functional neurons and glia in culture. Using subtractive hybridization, .apprx.1200 cDNA clones were isolated from ES cell cultures at the neural precursor stage of neural differentiation. Pilot studies indicated that this library is a good source of novel neuro-embryonic cDNA clones. Therefore, the entire library was screened by single-pass sequencing. Characterization of 604 non-redundant cDNA clones by BLAST revealed 96 novel expressed sequence tags (ESTs) and an addnl. 197 matching uncharacterized ESTs or genomic clones derived from genome sequencing projects. With the exception of a handful of genes, whose functions are still unclear, most of the 311 known genes identified in this screen are expressed in embryonic development and/or the nervous system. At least 80 of these genes are implicated in disorders of differentiation, neural development, and/or neural function. This study provides an initial snapshot of gene expression during early neural differentiation of ES cell cultures. Given the recent identification of human ES cells, further characterization of these novel and uncharacterized ESTs has the potential to identify genes that may be important in nervous system development, physiol., and disease.
OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 44 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:856761 CAPLUS
DOCUMENT NUMBER: 134:145499
TITLE: Regulation of a multigenic invasion program by the transcription factor, AP-1: re-expression of a down-regulated gene, TSC-36, inhibits invasion
AUTHOR(S): Johnston, Imogen M. P.; Spence, Heather J.; Winnie, Joseph N.; McGarry, Lynn; Vass, J. Keith; Meagher, Liam; Stapleton, Genevieve; Ozanne, Bradford W.
CORPORATE SOURCE: CRC Beatson Laboratories, Beatson Institute for Cancer Research, Glasgow, G61 1BD, UK
SOURCE: Oncogene (2000), 19(47), 5348-5358
CODEN: ONCNES; ISSN: 0950-9232

PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The transcription factor AP-1 (activator protein-1) is required for transformation by many oncogenes, which function upstream of it in the growth factor-ras signal transduction pathway. Previously, we proposed that one role of AP-1 in transformation is to regulate the expression of a multigenic invasion program. As a test of this proposal we sought to identify AP-1 regulated genes based upon their differential expression in 208F rat fibroblasts transformed by FBR-v-fos (FBR), and to determine if they functioned in the invasion program. Subtracted cDNA libraries specific for up- or down-regulated genes in FBRs compared to 208Fs were constructed and analyzed. Northern anal. revealed that the cDNAs in both libraries represented differentially expressed genes. Nucleic acid sequence anal. of randomly selected cDNA clones from each library coupled with searches of nucleic acid and amino acid sequence databases determined that many of the cDNAs represented proteins that function in various aspects of the invasion process. Functional anal. of one the down-regulated genes, TSC-36/follistatin-related protein (TSC-36/Frp), which has not previously been associated with invasion, demonstrated that its expression in FBRs inhibited in vitro invasion. These results support the proposal that AP-1 in transformed cells regulates a multigenic invasion program.
OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)
REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 45 OF 65 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:148677 CAPLUS
DOCUMENT NUMBER: 132:274003
TITLE: Sodium butyrate/retinoic acid costimulation induces apoptosis-independent growth arrest and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid
AUTHOR(S): Buommino, E.; Pasquali, D.; Sinisi, A. A.; Bellastella, A.; Morelli, F.; Metafora, S.
CORPORATE SOURCE: CNR International Institute of Genetics and Biophysics, Naples, Italy
SOURCE: Journal of Molecular Endocrinology (2000), 24(1), 83-94
CODEN: JMLEEI; ISSN: 0952-5041
PUBLISHER: Society for Endocrinology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retinoic acid (RA) and sodium butyrate (NaB) are regulators of cell growth and differentiation. We studied their effect on normal (SVC1) or v-Ki-ras-transformed (Ki-SVC1) rat seminal vesicle (SV) epithelial cell lines. The treatment of these cells with 10-7 M RA did not produce significant changes in the morphol. and biochem. parameters analyzed. When RA was used in combination with 2 mM NaB, the treatment induced substantial morphol. changes, apoptosis-independent growth arrest, up-regulation of tissue transglutaminase (tTGase), and down-regulation of β and γ RA receptor (RAR) mRNA expression. The same cells did not express RAR α either before or after NaB/RA treatment. A similar treatment did not change the amount of mRNA coding for the protein SV-IV (a typical differentiation marker of the SV epithelium) in normal or ras-transformed cells nor the level of v-Ki-ras mRNA in Ki-SVC1 cells. These findings suggest that a defective RA/RARs signaling pathway is probably the biochem. condition that underlies the unresponsiveness to RA of our in vitro culture system, and indirectly points to the possibility that the NaB/RA-induced effects were brought

about by a cooperation at the transcription level between the histone deacetylase inhibitory activity of NaB and the ability of RA/RAR to modulate the expression of various genes involved in the control of cell growth and differentiation.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 46 OF 65 MEDLINE on STN

ACCESSION NUMBER: 2005413048 MEDLINE

DOCUMENT NUMBER: PubMed ID: 16077937

TITLE: Mechanism of telomerase repression during terminal differentiation of normal epithelial cells and squamous carcinoma lines.

AUTHOR: Crowe David L; Nguyen Dan C; Ohannessian Arthur

CORPORATE SOURCE: Center for Craniofacial Molecular Biology, University of Southern California, Los Angeles, CA 90033, USA.. dcrowe@usc.edu

SOURCE: International journal of oncology, (2005 Sep) Vol. 27, No. 3, pp. 847-54. Journal code: 9306042. ISSN: 1019-6439.

PUB. COUNTRY: Greece

DOCUMENT TYPE: (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200509

ENTRY DATE: Entered STN: 4 Aug 2005 Last Updated on STN: 13 Sep 2005 Entered Medline: 12 Sep 2005

AB Stratified squamous epithelial cells undergo an orderly process of cell cycle arrest following detachment from the basement membrane. The basal layer cells which adhere to the basement membrane express telomerase, which maintains the ends of chromosomes in this rapidly dividing population. Non-dividing suprabasal cells downregulate telomerase activity. However, the mechanisms regulating this inhibition are unknown. We examined the regulation of telomerase expression in anchorage-deprived normal human epidermal keratinocytes and squamous cell carcinoma lines. Anchorage-deprived cells underwent rapid loss of telomerase activity. Attachment loss was associated with increased ERK1 activity, G1 to S phase progression, and subsequent G2 arrest. Adhesion to collagen via specific integrin subunits inhibited ERK1 activity and telomerase repression. Loss of telomerase expression was associated with recruitment of an Rb/HDAC1 repressor complex to the -98 E2F site of the hTERT promoter. We propose a mechanism by which anchorage deprivation inhibits telomerase activity in stratified squamous epithelial cells and squamous cell carcinoma lines.

L7 ANSWER 47 OF 65 MEDLINE on STN

ACCESSION NUMBER: 2001376276 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11319226

TITLE: Ca2+ and BMP-6 signaling regulate E2F during epidermal keratinocyte differentiation.

AUTHOR: D'Souza S J; Pajak A; Balazsi K; Dagnino L

CORPORATE SOURCE: Departments of Pharmacology/Toxicology and Paediatrics, Child Health Research Institute and Lawson Health Research Institute, University of Western Ontario, London, Ontario N6A 5C1, Canada.

SOURCE: The Journal of biological chemistry, (2001 Jun 29) Vol. 276, No. 26, pp. 23531-8. Electronic Publication: 2001-04-23.

Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20 Aug 2001
Last Updated on STN: 5 Jan 2003
Entered Medline: 16 Aug 2001

AB The epidermis consists of a squamous epithelium continuously replenished by committed stem cells, which can either self-renew or differentiate. We demonstrated previously that E2F genes are differentially expressed in developing epidermis (Dagnino, L., Fry, C. J., Bartley, S. M., Farnham, P., Gallie, B. L., and Phillips, R. A. (1997) Cell Growth Differ. 8, 553-563). Thus, we hypothesized that various E2F proteins likely play distinct growth regulatory roles in the undifferentiated stem cells and in terminally differentiated keratinocytes. To further understand the function of E2F genes in epidermal morphogenesis, we have examined the expression, regulation, and protein-protein interactions of E2F factors in undifferentiated cultured murine primary keratinocytes or in cells induced to differentiate with Ca(2+) or BMP-6 (bone morphogenetic protein 6). We find similar patterns of E2F regulation with both differentiating agents and demonstrate a switch in expression from E2F-1, -2, and -3 in undifferentiated, proliferating cells to E2F-5 in terminally differentiated keratinocytes. Inhibition of keratinocyte proliferation by transforming growth factor-beta1 did not enhance E2F-5 protein levels, suggesting that this response is specific to differentiation rather than reversible cell cycle withdrawal. E2F-5 up-regulation is also accompanied by formation of heteromeric nuclear complexes containing E2F5, p130, and histone deacetylase (HDAC) 1. Overexpression of E2F5 specifically inhibited DNA synthesis in undifferentiated keratinocytes in an HDAC-dependent manner, suggesting that E2F-5.p130.HDAC1 complexes are likely involved in the permanent withdrawal from the cell cycle of keratinocytes responding to differentiation stimuli.

L7 ANSWER 48 OF 65 MEDLINE on STN
ACCESSION NUMBER: 2001069352 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10938272
TITLE: Rapid induction of histone hyperacetylation and cellular differentiation in human breast tumor cell lines following degradation of histone deacetylase-1.
AUTHOR: Zhou Q; Melkoumian Z K; Lucktong A; Moniwa M; Davie J R; Strobl J S
CORPORATE SOURCE: Department of Pharmacology & Toxicology, Robert C. Byrd Health Sciences Center, West Virginia University, Morgantown, West Virginia 26506, USA.
SOURCE: The Journal of biological chemistry, (2000 Nov 10) Vol. 275, No. 45, pp. 35256-63.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 4 Jan 2001

AB Quinidine inhibits proliferation and promotes cellular differentiation in human breast tumor epithelial cells. Previously we showed quinidine arrested MCF-7 cells in G(1) phase of the cell cycle and led to a G(1) to G(0) transition followed by apoptotic cell death. The present experiments demonstrated that MCF-7, MCF-7ras, T47D, MDA-MB-231, and MDA-MB-435 cells transiently differentiate before undergoing apoptosis in response to quinidine. The cells accumulated lipid droplets, and the cytokeratin 18 cytoskeleton was reorganized. Hyperacetylated histone H4 appeared within 2 h of the addition of quinidine to the medium, and levels were maximal by 24 h. Quinidine-treated MCF-7 cells showed elevated p21(WAF1), hypophosphorylation and suppression of retinoblastoma protein, and down-regulation of cyclin D1, similar to the cell cycle response observed with cells induced to differentiate by histone deacetylase inhibitors, trichostatin A, and trapoxin. Quinidine did not show evidence for direct inhibition of histone deacetylase enzymatic activity in vitro. HDAC1 was undetectable in MCF-7 cells 30 min after addition of quinidine to the growth medium. The proteasome inhibitors MG-132 and lactacystin completely protected HDAC1 from the action of quinidine. We conclude that quinidine is a breast tumor cell differentiating agent that causes the loss of HDAC1 via a proteasomal sensitive mechanism.

L7 ANSWER 49 OF 65 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:120165 BIOSIS
DOCUMENT NUMBER: PREV200200120165
TITLE: Beyond tamoxifen new endpoints for breast cancer chemoprevention, new drugs for breast cancer prevention.
AUTHOR(S): Fabian, Carol J. [Reprint author]; Kimler, Bruce F.
CORPORATE SOURCE: University of Kansas Medical Center, Rainbow Boulevard, Kansas City, KS, 66160-7320, USA
cfabian@kumc.edu
SOURCE: Osborne, Michael P. [Editor]. Ann. N. Y. Acad. Sci., (2001) pp. 44-59. Annals of the New York Academy of Sciences. Cancer prevention: Molecular mechanisms to clinical applications. print.
Publisher: New York Academy of Sciences, 2 East 63rd Street, New York, NY, 10021, USA. Series: Annals of the New York Academy of Sciences.
Meeting Info.: Conference on Cancer Prevention: Molecular Mechanisms to Clinical Applications. New York, New York, USA. November 10-11, 2000.
CODEN: ANYAA9. ISSN: 0077-8923. ISBN: 1-57331-350-5 (cloth), 1-57331-351-3 (paper).
DOCUMENT TYPE: Book
Conference; (Meeting)
Book; (Book Chapter)
Conference; (Meeting Paper)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 2002
Last Updated on STN: 26 Feb 2002

L7 ANSWER 50 OF 65 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2007073421 EMBASE
TITLE: Advances in the biology of lung cancer chemoprevention.
AUTHOR: Hirsch, Fred R., Dr. (correspondence)
CORPORATE SOURCE: University of Colorado Cancer Center, 12801 E. 17th Avenue, Aurora, CO 80010, United States. Fred.Hirsch@uchsc.edu
AUTHOR: Lippman, Scott M.
SOURCE: Journal of Clinical Oncology, (2005) Vol. 23, No. 14, pp. 3186-3197.

Refs: 104
ISSN: 0732-183X CODEN: JCONDN
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 28 Mar 2007
Last Updated on STN: 28 Mar 2007

AB The heavy burden of lung cancer, which includes the highest worldwide mortality of any cancer, and its resistance to standard approaches (smoking cessation, screening, and therapy), have motivated an intense interest in chemoprevention of this disease. Randomized controlled trials of agents (including retinoids, beta-carotene, and vitamin E) to prevent lung cancer have produced only disappointing clinical results to date. New, molecular-targeted approaches are advancing rapidly, however, with many promising targets and interactive signaling pathways for developing novel agents and combinatorial approaches in this setting. This promise is illustrated by recent studies of 15-hydroxyprostaglandin dehydrogenase, which plays a critical role in polyunsaturated fatty acid metabolism and (like another important target, prostacyclin) is downstream of cyclooxygenase-2. 15-hydroxyprostaglandin dehydrogenase degrades prostaglandin E2, appears to have tumor suppressor activity, and can be induced both by peroxisome proliferator- activated receptor-gamma ligands and an epidermal growth factor receptor inhibitor. Other important targets/pathways include the insulin-like growth factor axis, phosphoinositide 3-kinase pathway, cyclin D and E family members, and epigenetic events. Defining highest lung cancer risk (eg, establishing molecular risk models through long-term analyses of high-risk cohorts) will facilitate the clinical development of molecular-targeted prevention that will potentially reduce the enormous burden of lung cancer. .COPYRGT. 2005 by American Society of Clinical Oncology.

L7 ANSWER 51 OF 65 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006294841 EMBASE
TITLE: Targeted therapies for non-small cell lung cancer.
AUTHOR: Spicer, J.; Harper, Peter (correspondence)
CORPORATE SOURCE: Guy's Hospital, St. Thomas Street, London SE1 9RT, United Kingdom. peter.harper@kcl.ac.uk
SOURCE: International Journal of Clinical Practice, (Sep 2005) Vol. 59, No. 9, pp. 1055-1062.
Refs: 58
ISSN: 1368-5031; E-ISSN: 1742-1241 CODEN: IJCPF9
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Jul 2006
Last Updated on STN: 3 Jul 2006

AB Despite recent advances in current chemotherapy, the prognosis for locally advanced and metastatic nonsmall-cell cancer remains poor, and new approaches are required. An increased understanding of the biology of

lung cancer has identified pathways mediated by receptor tyrosine kinases as an important target. The epidermal growth factor receptor (EGFR) is frequently expressed on the surface of the lung cancer cell. EGFR can be targeted by inhibitors of receptor tyrosine kinase activity such as erlotinib and gefitinib and by antibodies specific for the extracellular domain. Subset analysis of responders to the receptor tyrosine kinase inhibitors suggests that clinical benefit may correlate with the presence of EGFR mutations. Other drugs in earlier clinical development include those directed against HER-2, VEGF, farnesyl transferase, COX-2 and retinoid receptor. .COPYRGT. Blackwell Publishing Ltd, 2005.

L7 ANSWER 52 OF 65 EMBASE

ACCESSION NUMBER: 2005583450 EMBASE

TITLE: Analysis of BCL6-interacting proteins by tandem mass spectrometry.

AUTHOR: Miles, Rodney R.; Lim, Megan S. (correspondence); Elenitoba-Johnson, Kojo S.J.

CORPORATE SOURCE: Department of Pathology, University of Utah, School of Medicine, 50 North Medical Dr., Salt Lake City, UT 84132, United States. kojo.elenitobaj@path.utah.edu; megan.lim@path.utah.edu

AUTHOR: Crockett, David K.; Lim, Megan S. (correspondence); Elenitoba-Johnson, Kojo S.J.

CORPORATE SOURCE: ARUP Institute for Clinical and Experimental Pathology, Salt Lake City, UT 84108, United States. kojo.elenitobaj@path.utah.edu; megan.lim@path.utah.edu

AUTHOR: Lim, Megan S. (correspondence)

CORPORATE SOURCE: Dept. of Pathology, University of Utah, School of Medicine, 50 North Medical Dr., Salt Lake City, UT 84132, United States. megan.lim@path.utah.edu

SOURCE: Molecular and Cellular Proteomics, (Dec 2005) Vol. 4, No. 12, pp. 1898-1909.
Refs: 34
ISSN: 1535-9476 CODEN: MCPOBS

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jan 2006
Last Updated on STN: 12 Jan 2006

AB B-cell lymphoma 6 (BCL6) is a 95-kDa nuclear phosphoprotein and member of the Pox virus zinc finger/bric-a-brac, tramtrack, broad complex (POZ/BTB) family of transcription factors. BCL6 is a transcriptional repressor required for germinal center formation, and the gene encoding it is frequently altered in diffuse large B-cell and follicular lymphomas. The dysregulation of BCL6 has therefore been implicated in lymphomagenesis. A limited number of proteins is known to interact with BCL6 and modulate its activity or participate in its role in transcriptional regulation. Identification of additional BCL6-binding proteins could reveal potential signaling targets and previously undescribed functional roles for BCL6. We used a functional proteomic approach to determine the identity of proteins that interact with BCL6. Proteins were isolated by co-immunoprecipitation with an anti-BCL6 antibody and identified using MS/MS. We identified 61 proteins in the BCL6 immunocomplex from the following Gene Ontology categories: transcription regulator activity (n = 18), binding activity (n = 11), signal transducer activity (n = 10), catalytic activity (n = 8), structural molecule activity (n = 3), enzyme regulator activity (n = 3), transporter activity (n = 2), motor activity (n = 2), chaperone activity (n = 1), and unknown function (n = 3).

Importantly we identified BCL6 and several previously reported BCL6-interacting proteins in the BCL6 immunocomplex. The remaining proteins have not been shown previously to be associated with BCL6. MS/MS results were validated on four proteins using immunoprecipitation and Western blotting. Two of these protein interactions were further confirmed by reciprocal immunoprecipitation. This study demonstrates the utility of antibody immunoprecipitation and subsequent peptide identification by MS/MS for the elucidation of BCL6-binding proteins. Many of the novel proteins identified in this study suggest additional functional roles for BCL6 beyond transcriptional repression. .COPYRGT. 2005 by The American Society for Biochemistry and Molecular Biology, Inc.

L7 ANSWER 53 OF 65 EMBASE

ACCESSION NUMBER: 2005567251 EMBASE
TITLE: cDNA microarray-based translational research in soft tissue sarcoma.
AUTHOR: Lubieniecka, Joanna M.; Nielsen, Torsten O., Dr. (correspondence)
CORPORATE SOURCE: Vancouver Coastal Health Research Institute, Department of Pathology, University of British Columbia, Vancouver, BC, Canada. torsten@interchange.ubc.ca
AUTHOR: Nielsen, Torsten O., Dr. (correspondence)
CORPORATE SOURCE: Anatomical Pathology, Vancouver Hospital, 855 West 12th Avenue, Vancouver, BC V5Z1M9, Canada. torsten@interchange.ubc.ca
SOURCE: Journal of Surgical Oncology, (15 Dec 2005) Vol. 92, No. 4, pp. 267-271.
Refs: 53
ISSN: 0022-4790 CODEN: JSONAU
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
022 Human Genetics
030 Clinical and Experimental Pharmacology
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jan 2006
Last Updated on STN: 12 Jan 2006
AB The authors discuss application of cDNA microarray technology in translational research to identify diagnostic markers and therapeutic targets in adult soft tissue sarcoma. Recent results in synovial sarcoma are used to highlight the applicability of this technology for marker and target discovery, as well as the need for preclinical validation of putative therapeutic targets. .COPYRGT. 2005 Wiley-Liss, Inc.

L7 ANSWER 54 OF 65 EMBASE

ACCESSION NUMBER: 2005493518 EMBASE
TITLE: Cancer chemoprevention: Scientific promise, clinical uncertainty.
AUTHOR: Sporn, Michael B, Prof. (correspondence)
CORPORATE SOURCE: Deparment of Pharmacology, Dartmouth Medical School, Hanover, NH 03755, United States. michael.b.sporn@dartmouth.edu
AUTHOR: Liby, Karen T.
CORPORATE SOURCE: Dartmouth Medical School, Hanover, NH 03755, United States.
SOURCE: Nature Clinical Practice Oncology, (Oct 2005) Vol. 2, No. 10, pp. 518-525.
Refs: 64

ISSN: 1743-4254; E-ISSN: 1743-4262
PUBLISHER IDENT.: N0319
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Nov 2005
Last Updated on STN: 17 Nov 2005

AB We review fundamental processes, such as mutation, oxidative stress, and inflammation that are critical for carcinogenesis and provide specific molecular targets for new chemopreventive agents. New information from molecular biology studies has identified such targets, including regulatory molecules such as Nrf2 (nuclear factor erythroid 2-related factor 2), epidermal growth factor receptor kinases, phosphatidylinositol 3-kinase, components of the Janus kinase-signal transducers and activators of transcription (JAK -STAT) pathway, nuclear factor-κB, and cyclin D. The development of new drugs for the control of these targets that are both safe and effective will be important for the future of cancer chemoprevention. .COPYRGT. 2005 Nature Publishing Group.

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ACCESSION NUMBER: 2005427962 EMBASE
TITLE: Gefitinib (Iressa) in oncogene-addictive cancers and therapy for common cancers.
AUTHOR: Blagosklonny, Mikhail V. (correspondence)
CORPORATE SOURCE: Brander Cancer Research Institute, New York Medical College, 19 Bradhurst Ave., Hawthorne, NY 10532, United States. m_blagosklonny@nymc.edu
SOURCE: Cancer Biology and Therapy, (May 2004) Vol. 3, No. 5, pp. 436-440.
Refs: 66
ISSN: 1538-4047; E-ISSN: 1555-8576
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Oct 2005
Last Updated on STN: 27 Oct 2005

AB Activating mutations in the epidermal growth factor receptor (EGF-R) predict response to gefitinib. How does this recent discovery affect our outlook on selective (targeted) cancer therapy? It allows us to compare mutant EGF-R with Bcr-Abl as anticancer drug targets and to discuss the nature of oncogene addiction. It emphasizes molecular diagnostics to identify oncogene-addictive cancers. It also re-enforces the notion that most cancers with multiple oncogenic alterations (common cancers) will unlikely respond to selective drugs alone. In such cancers, one strategy is targeting cancer-non-specific, universal and vital structures, essential for life of all cells: microtubules, topoisomerases, histone deacetylases, the proteasome. But in order to be cancer-selective, these chemotherapeutic agents need to be combined with selective agents. Such combinations can be effective and selective in common cancers. .COPYRGT.2004 Landes Bioscience.

L7 ANSWER 56 OF 65 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005100877 EMBASE
TITLE: Nonclassical retinoids and lung carcinogenesis.
AUTHOR: Dragnev, Konstantin H., Dr. (correspondence); Petty, W. Jeffrey; Rigas, James R.; Dmitrovsky, Ethan
CORPORATE SOURCE: Department of Medicine, Dartmouth-Hitchcock Medical Center, Hanover, NH, United States. dragnev@dartmouth.edu
AUTHOR: Dragnev, Konstantin H., Dr. (correspondence); Rigas, James R.; Dmitrovsky, Ethan
CORPORATE SOURCE: Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Hanover, NH, United States. dragnev@dartmouth.edu
AUTHOR: Ma, Yan; Dmitrovsky, Ethan
CORPORATE SOURCE: Dept. of Pharmacology and Toxicology, Dartmouth Medical School, Lebanon, NH, United States.
AUTHOR: Dragnev, Konstantin H., Dr. (correspondence)
CORPORATE SOURCE: Hematology/Oncology Section, Dartmouth-Hitchcock Medical Center, One Medical Center, Lebanon, NH 03756, United States. dragnev@dartmouth.edu
SOURCE: Clinical Lung Cancer, (Jan 2005) Vol. 6, No. 4, pp. 237-244.
Refs: 95
ISSN: 1525-7304 CODEN: CLCLCA
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2005
Last Updated on STN: 17 Mar 2005

AB The retinoids are natural and synthetic derivatives of vitamin A. These cancer therapeutic and chemopreventive agents exert antiproliferative, differentiation-inducing, proapoptotic, and other biologic effects. The retinoids act through nuclear retinoid receptors to activate target genes that signal biologic effects. Agents that specifically activate the nuclear retinoid X receptors (RXRs) are known as rexinoids. Rexinoid growth suppression of human bronchial epithelial cells was linked to triggering of G1 cell cycle arrest, concomitant growth suppression, and a decrease in expression of G1 cyclins through activation of a proteasome-dependent degradation pathway. Clinical studies have demonstrated prolonged survival of subsets of patients with non-small-cell lung cancer (NSCLC) treated with rexinoids as single agents or as part of combination regimens. The critical role of RXR in downstream signaling makes rexinoids especially attractive agents to consider in combination therapy. There is encouraging evidence for therapeutic benefit of combination regimens of rexinoids with other targeted agents, such as epidermal growth factor receptor inhibitors, and with chemotherapy. Results from randomized phase III clinical trials in NSCLC will ultimately determine the impact for rexinoid-based therapy or chemoprevention for lung cancer.

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ACCESSION NUMBER: 2004510527 EMBASE
TITLE: A novel computational approach for the prediction of networked transcription factors of aryl hydrocarbon-receptor-regulated genes.
AUTHOR: Kel, Alexander; Matys, Volker; Wingender, Edgar

CORPORATE SOURCE: BIOBASE GmbH, Wolfenbuttel, Germany.
AUTHOR: Kel, Alexander
CORPORATE SOURCE: Institute of Cytology and Genetics, Novosibirsk, Russian Federation.
AUTHOR: Reymann, Susanne; Borlak, Jurgen, Dr. (correspondence)
CORPORATE SOURCE: Fraunhofer Inst. Toxicol./Exp. Med., Ctr. for Drug Res. and Med. Biotech., Nikolai-Fuchs-Str. 1, D-30625 Hannover, Germany. borlak@item.fraunhofer.de
AUTHOR: Nettesheim, Paul
CORPORATE SOURCE: Natl. Inst. of Environ. Hlth. Sci., Research Triangle Park, NC, United States.
AUTHOR: Borlak, Jurgen, Dr. (correspondence)
CORPORATE SOURCE: Ctr. of Pharmacology and Toxicology, Medical School of Hannover, Hannover, Germany. borlak@item.fraunhofer.de
SOURCE: Molecular Pharmacology, (Dec 2004) Vol. 66, No. 6, pp. 1557-1572.
Refs: 29
ISSN: 0026-895X CODEN: MOPMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 28 Dec 2004
Last Updated on STN: 28 Dec 2004

AB A novel computational method based on a genetic algorithm was developed to study composite structure of promoters of coexpressed genes. Our method enabled an identification of combinations of multiple transcription factor binding sites regulating the concerted expression of genes. In this article, we study genes whose expression is regulated by a ligand-activated transcription factor, aryl hydrocarbon receptor (AhR), that mediates responses to a variety of toxins. AhR-mediated change in expression of AhR target genes was measured by oligonucleotide microarrays and by reverse transcription-polymerase chain reaction in human and rat hepatocytes. Promoters and long-distance regulatory regions (>10 kb) of AhR-responsive genes were analyzed by the genetic algorithm and a variety of other computational methods. Rules were established on the local oligonucleotide context in the flanks of the AhR binding sites, on the occurrence of clusters of AhR recognition elements, and on the presence in the promoters of specific combinations of multiple binding sites for the transcription factors cooperating in the AhR regulatory network. Our rules were applied to search for yet unknown Ah-receptor target genes. Experimental evidence is presented to demonstrate high fidelity of this novel in silico approach.

L7 ANSWER 58 OF 65 EMBASE
ACCESSION NUMBER: 2004265445 EMBASE
TITLE: Heregulin regulates the ability of the ErbB3-binding protein Ebp1 to bind E2F promoter elements and repress E2F-mediated transcription.
AUTHOR: Zhang, Yuexing; Hamburger, Anne W. (correspondence)
CORPORATE SOURCE: Greenebaum Cancer Center, Univ. of Maryland School of Medicine, Baltimore, MD 21201, United States. ahamburg@som.umaryland.edu
AUTHOR: Zhang, Yuexing; Hamburger, Anne W. (correspondence)
CORPORATE SOURCE: Department of Pathology, Univ. of Maryland School of Medicine, Baltimore, MD 21201, United States. ahamburg@som.umaryland.edu
AUTHOR: Hamburger, Anne W. (correspondence)
CORPORATE SOURCE: Greenebaum Cancer Center, University of Maryland at

Baltimore, BRB 9-047, 655 W. Baltimore St., Baltimore, MD 21201, United States. ahamburg@som.umaryland.edu
SOURCE: Journal of Biological Chemistry, (18 Jun 2004) Vol. 279, No. 25, pp. 26126-26133.
Refs: 40
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 22 Jul 2004
Last Updated on STN: 22 Jul 2004

AB The ErbB3/4 ligand heregulin (HRG) profoundly affects cell growth and differentiation, but its mechanism of action is poorly understood. Ebp1, a protein isolated by its binding to ErbB3, inhibits cell growth and represses transcription of E2F-regulated cell cycle genes. Since Ebp1 shares 38% identity with a Schizosaccharomyces pombe DNA-binding protein, we postulated that Ebp1 could bind E2F consensus elements in an HRG-inducible manner, leading to transcriptional repression. We show here that GST-Ebp1 bound to the DNA sequence bound by the S. pombe protein. Whereas GST-Ebp1 alone failed to bind E2F1 promoter elements, Ebp1 contained in nuclear lysates associated with E2F1 consensus sequences in the E2F1 promoter. Endogenous Ebp1 was recruited to the E2F1 promoter in vivo as demonstrated by chromatin immunoprecipitation assays. Ebp1 bound E2F consensus oligonucleotides in association with E2F1, retinoblastoma protein, and HDAC2. HRG regulated the association of Ebp1 with E2F promoter sequences and enhanced the ability of Ebp1 to repress transcription. Our findings suggest that Ebp1, by linking HRG activation of membrane receptors to E2F gene activity, may be a downstream modulator of the effects of HRG on cell cycle progression.

L7 ANSWER 59 OF 65 EMBASE
ACCESSION NUMBER: 2004169370 EMBASE
TITLE: Focus on head and neck cancer.
AUTHOR: Mao, Li (correspondence); Hong, Waun K.; Papadimitrakopoulou, Vassiliki A.
CORPORATE SOURCE: Dept. Thorac./Hd. Neck Med. Oncol., Univ. Texas M.D. Anderson Cancer C., Univ. Texas Grad. Sch. Biomed. S., Houston, TX 77030, United States. lmao@mdanderson.org
SOURCE: Cancer Cell, (Apr 2004) Vol. 5, No. 4, pp. 311-316.
Refs: 58
ISSN: 1535-6108 CODEN: CCAECI
PUBLISHER IDENT.: S 1535-6108(04)00090-X
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 011 Otorhinolaryngology
016 Cancer
022 Human Genetics
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 6 May 2004
Last Updated on STN: 6 May 2004

L7 ANSWER 60 OF 65 EMBASE
ACCESSION NUMBER: 2004022333 EMBASE
TITLE: The Insulin-like Growth Factors and Insulin-signalling Systems: An Appealing Target for Breast Cancer Therapy?.
AUTHOR: Gray, S.G., Dr. (correspondence); De Meyts, P.

CORPORATE SOURCE: Receptor Biology Laboratory, Hagedorn Research Institute, Niels Steensens Vej 6, DK 2820 Gentofte, Denmark. stvg@novonordisk.com
AUTHOR: Stenfeldt Mathiasen, I.
CORPORATE SOURCE: Dept. of Cancer and Immunobiology, Novo Nordisk A/S, Malov, Denmark.
SOURCE: Hormone and Metabolic Research, (Nov 2003) Vol. 35, No. 11-12, pp. 857-871.
Refs: 100
ISSN: 0018-5043 CODEN: HMMRA2
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
029 Clinical and Experimental Biochemistry
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 20 Feb 2004
AB There is compelling evidence from epidemiological studies in humans, as well as in vitro and in vivo experimental observations including transgenic animal models, for a role of the IGF/insulin signalling system in cancer tumourigenesis. In this review focused on breast cancer, we review the experimental evidence, discuss the cellular and molecular mechanisms of tumourigenicity by the IGFs and insulin and various possible therapeutic strategies based on the mechanisms discussed.

L7 ANSWER 61 OF 65 EMBASE
ACCESSION NUMBER: 2003427785 EMBASE
TITLE: Chemoprevention of tumors: The role of RAR-beta.
AUTHOR: Toma, Salvatore, Dr. (correspondence); Spadini, N.
CORPORATE SOURCE: Dept. of Oncol. Biol./Genetics, University of Genoa, Genoa, Italy. toma@cba.unige.it
AUTHOR: Toma, Salvatore, Dr. (correspondence); Emionite, L.; Fabia, G.
CORPORATE SOURCE: Natl. Inst. for Cancer Res. (IST), Genoa, Italy. toma@cba.unige.it
AUTHOR: Spadini, N.; Vergani, L.
CORPORATE SOURCE: Dept. of Biophys. Sci./Technol. M/O, University of Genoa, Genoa, Italy.
AUTHOR: Toma, Salvatore, Dr. (correspondence)
CORPORATE SOURCE: Dept. of Oncol. Biol. and Genet., University of Genova, National Institute for Cancer Res., Largo Rosanna Benzi 10, 16132 Genova, Italy. toma@cba.unige.it
SOURCE: International Journal of Biological Markers, (Jan 2003) Vol. 18, No. 1, pp. 78-81.
Refs: 32
ISSN: 0393-6155 CODEN: IBMAEP
COUNTRY: Italy
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 014 Radiology
016 Cancer
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Nov 2003
Last Updated on STN: 6 Nov 2003

AB Chemoprevention can be defined as the use of specific natural or synthetic chemical agents to reverse, suppress, or prevent carcinogenic progression to invasive cancer. The knowledge of carcinogenic mechanisms provides the scientific rationale for chemoprevention. Epithelial carcinogenesis proceeds through multiple discernible stages of molecular and cellular alterations. Understanding of the multistep nature of carcinogenesis has evolved through highly controlled animal carcinogenesis studies, and these studies have identified three distinct phases: initiation, promotion and progression. Animal model studies have provided evidence that the development of cancer involves many different factors, including alterations in the structures and functions of different genes. Transitions between successive stages can be enhanced or inhibited in the laboratory by different types of agents, such activities providing the fundamental basis for chemoprevention.

L7 ANSWER 62 OF 65 EMBASE

ACCESSION NUMBER: 2003051191 EMBASE
TITLE: Lung cancer prevention: The guidelines.
AUTHOR: Dragnev, Konstantin H., Dr. (correspondence); Dmitrovsky, Ethan
CORPORATE SOURCE: Norris Cotton Cancer Center, Lebanon, NH, United States. dragnev@dartmouth.edu
AUTHOR: Stover, Diane
CORPORATE SOURCE: Pulmonary Section, Department of Medicine, Mem. Sloan-Kettering Cancer Center, New York, NY, United States.
AUTHOR: Dragnev, Konstantin H., Dr. (correspondence)
CORPORATE SOURCE: Hematology/Oncology Section, Department of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH 03756, United States. dragnev@dartmouth.edu
SOURCE: Chest, (2003) Vol. 123, No. 1 SUPPL., pp. 60S-71S.
Refs: 81
ISSN: 0012-3692 CODEN: CHETBF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
017 Public Health, Social Medicine and Epidemiology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Feb 2003
Last Updated on STN: 7 Feb 2003
AB Lung carcinogenesis is a chronic and multi-step process resulting in malignant lung tumors. This progression from normal to neoplastic pulmonary cells or tissues could be arrested or reversed through pharmacologic treatments, which are known as cancer chemoprevention. These therapeutic interventions should reduce or avoid the clinical consequences of lung cancer by treating early neoplastic lesions before the development of clinically evident signs or symptoms of malignancy. Preclinical, clinical, and epidemiologic findings relating to different classes of candidate chemopreventive agents provide strong support for lung cancer prevention as an attractive therapeutic strategy. Smoking prevention and smoking cessation represent an essential approach to reduce the societal impact of tobacco carcinogenesis. However, even if all the goals of the national antismoking efforts were met, there still would be a large population of former smokers who would be at increased risk for lung cancers. Lung cancer also can occur in those persons who never have smoked. This article focuses on what is now known about pharmacologic strategies for lung cancer prevention. Randomized clinical trials using β-carotene, retinol, isotretinoin or N-acetyl-cysteine did

not show benefit for primary and tertiary lung cancer prevention. There is also evidence that the use of β-carotene and isotretinoin for lung cancer chemoprevention in high-risk individuals may increase the risk for lung cancer, especially in individuals who continue to smoke. There is a need for relevant in vitro models to identify pathways that activate chemopreventive effects in the lung. An improved understanding of cancer prevention mechanisms should aid in the design of clinical trials and in the validation of candidate chemopreventive targets as well as the discovery of new targets. Until such studies are completed, no agent or combination of agents should be used for lung cancer prevention outside of a clinical trial.

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ACCESSION NUMBER: 2003045790 EMBASE
TITLE: The biology of breast carcinoma.
AUTHOR: Keen, Judith Clancy; Davidson, Nancy E., Dr. (correspondence)
CORPORATE SOURCE: Sidney Kimmel Compreh. Cancer Center, Johns Hopkins School of Medicine, 1650 Orleans Street, Baltimore, MD 21231, United States. davidna@jhmi.edu
SOURCE: Cancer, (1 Feb 2003) Vol. 97, No. 3 SUPPL., pp. 825-833.
Refs: 107
ISSN: 0008-543X CODEN: CANCAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 2004
Last Updated on STN: 20 Feb 2004

AB The biology of breast carcinoma is complex, with multiple factors contributing to its development and progression. The current review focuses on the role of several critical genes including estrogen receptor, progesterone receptor, retinoic acid receptor-β, epidermal growth factor receptor family members, p53, BRCA1, and BRCA2 as risk factors for the development of disease, predictors of prognosis and response to therapy, and as therapeutic targets. Studies of the biology of these and other genes that contribute to the development and progression of breast carcinoma have had and will continue to have great impact on all aspects of disease management. .COPYRGT. 2003 American Cancer Society.

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ACCESSION NUMBER: 2002025794 EMBASE
TITLE: Beyond tamoxifen: New endpoints for breast cancer chemoprevention, new drugs for breast cancer prevention.
AUTHOR: Fabian, Carol J., Dr. (correspondence); Kimler, Bruce F.
CORPORATE SOURCE: University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160-7320, United States. cfabian@kumc.edu
SOURCE: Annals of the New York Academy of Sciences, (2001) Vol. 952, pp. 44-59.
Refs: 113
ISSN: 0077-8923 CODEN: ANYAA9
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology

037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 2002
Last Updated on STN: 31 Jan 2002

AB Although tamoxifen appears to markedly reduce breast cancer risk in women with a prior diagnosis of atypical hyperplasia or in situ carcinoma, it is not clear what other groups of women receive substantial benefit. Major breast chemoprevention priorities are to (1) develop new agents that (a) have fewer side effects, (b) are effective in ER - as well as tamoxifen-resistant precancerous tissue, and (c) are compatible with hormone therapy; and (2) develop efficient clinical strategies including prognostic and predictive morphologic and molecular biomarkers. Breast tissue may be repeatedly sampled for evidence of intraepithelial neoplasia by fine needle aspiration, ductal lavage, or needle biopsy to select candidates at highest short-term risk as well as to monitor response in small proof of principle studies prior to a large cancer incidence trial. Molecular marker expression may also be used to select a cohort most likely to respond to a particular agent. A large number of new agents are attractive as potential prevention agents and some are already in clinical prevention testing. Compounds which should be effective in ER + precancerous tissue but may have a better side-effect profile include new selective estrogen receptor modulators which lack uterine estrogen agonist activity, isoflavones, aromatase inactivators/inhibitors for postmenopausal women, and gonadotropin-releasing hormone regimens for premenopausal women. Retinoids, rexinoids, and deltanoids may be efficacious in ER + tissue resistant to tamoxifen. Agents which should theoretically have activity in ER - or ER + precancerous tissue include polyamine synthesis inhibitors, tyrosine kinase inhibitors, combined demethylating agents and histone deacetylase inhibitors, as well as metalloprotease and angiogenesis inhibitors. Sample Phase I and Phase II clinical trial designs are reviewed using modulation of molecular markers and breast intraepithelial neoplasia as the major endpoints.

L7 ANSWER 65 OF 65 EMBASE
ACCESSION NUMBER: 2001330966 EMBASE
TITLE: Lung cancer chemoprevention: An integrated approach.
AUTHOR: Lippman, S.M., Dr. (correspondence); Spitz, M.R.
CORPORATE SOURCE: Anderson Cancer Center, Dept. of Clinical Cancer Prevention, Box 236, 1515 Holcombe Blvd, Houston, TX 77030, United States. slippman@mdanderson.org
SOURCE: Journal of Clinical Oncology, (15 Sep 2001) Vol. 19, No. 18 SUPPL., pp. 74s-82s.
Refs: 87
ISSN: 0732-183X CODEN: JCONDN
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Oct 2001
Last Updated on STN: 11 Oct 2001

AB Lung cancer is the leading cause of cancer deaths in the United States and the world, with grim incidence and mortality figures underscoring the need for new approaches, such as chemoprevention, for controlling this disease. There have been definitive, randomized, controlled lung-cancer chemoprevention trials in the three chemoprevention trial settings:

primary (healthy high-risk [eg, smokers]), secondary (premalignant lesions), and tertiary (prevention of second primary tumors in previously treated patients), all of which produced negative (either neutral or harmful) primary end point results. These trials established that lung cancer was not prevented by alpha-tocopherol, beta-carotene, retinol, retinyl palmitate, N-acetylcysteine, or isotretinoin in smokers. Provocative leads of the definitive trials include the possible activity of isotretinoin in never and former smokers and that of alphatocopherol in prostate cancer prevention. A major area of lung cancer research is molecular epidemiologic study of highest smoking-related risk based on the interactions between tobacco carcinogens, genetic polymorphisms involved in activating and detoxifying these carcinogens, and host-cell efficiency in monitoring and repairing tobacco carcinogen-DNA damage. The future of lung cancer chemoprevention will rely heavily on molecular studies of carcinogenesis and drug mechanisms to develop novel chemopreventive targets and drugs, risk markers, and surrogate end point biomarkers; new preclinical drug-testing models; novel imaging techniques for monitoring agent activity; and molecular epidemiologic risk models for identifying the highest-risk current and former smokers.

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                  U.S. patents
 NEWS  6  SEP 09  50 Millionth Unique Chemical Substance Recorded in
                  CAS REGISTRY
 NEWS  7  SEP 11  WPIDS, WPINDEX, and WPIX now include Japanese FTERM
                  thesaurus
 NEWS  8  OCT 21  Derwent World Patents Index Coverage of Indian and
                  Taiwanese Content Expanded
 NEWS  9  OCT 21  Derwent World Patents Index enhanced with human
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                  Utility Models
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L3 44 L2 NOT PY>2004

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L3 ANSWER 1 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:397214 CAPLUS
DOCUMENT NUMBER: 143:71194
TITLE: Molecular profiling of embryonal carcinoma cells following retinoic acid or histone deacetylase inhibitor treatment
AUTHOR(S): Sangster-Guity, Niquiche; Yu, Li-Ming; McCormick, Paulette
CORPORATE SOURCE: Department of Biological Sciences, University at Albany, Albany, NY, USA
SOURCE: Cancer Biology & Therapy (2004), 3(11), 1109-1120
CODEN: CBTAAO; ISSN: 1538-4047
PUBLISHER: Landes Bioscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Regulation of tissue homeostasis is crucial to disease prevention; cell division, cell cycle arrest, differentiation and apoptosis have to be tightly controlled in order to maintain this homeostasis. Retinoic acid (RA) and the histone deacetylase inhibitors (HDACIs) have profound effects on these processes and thus may be critical regulators of homeostasis. Consequently, RA and/or histone deacetylase inhibitors are currently being tested in clin. trials for a variety of cancers. Unfortunately, little is known of the overall affect of these compds. on cellular gene expression. Therefore, we decided to compare the effects of all-trans retinoic acid (ATRA) and a particular HDACI-Trichostatin A (TSA)-on an embryonal carcinoma (EC) cell line (F9) using gene chip anal. We have focused particular attention on those genes that may be differentially affected by these compds. Within the parameters established for this study, only 116 of the 12,488 genes examined were similarly regulated by ATRA and TSA: 75 pos. and 41 neg. An addnl. 70 genes were affected by only one of the compds. and 19 genes were actually inversely regulated. The gene set inversely regulated by ATRA and TSA includes several important patterning genes as well as the crucial tumor suppressor/promoter, transforming growth factor beta 1 (TGFβ1). Promoter anal. suggests a motif that may regulate one set of these genes. This study provides the first comprehensive comparison of global gene expression on EC cells as affected by ATRA and a HDAC inhibitor (TSA); reveals new targets for ATRA and HDAC inhibitors; identifies a new regulatory motif; demonstrates that ATRA and HDAC inhibitors do not always act synergistically on gene expression; and examines particular questions regarding their concurrent clin. application.
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:218654 CAPLUS
DOCUMENT NUMBER: 143:533
TITLE: Histone deacetylase

inhibitors enhance retinoid response in human breast cancer cell lines

AUTHOR(S): Emionite, Laura; Galmozzi, Fabia; Grattarola, Myriam; Boccardo, Francesco; Vergani, Laura; Toma, Salvatore

CORPORATE SOURCE: Department of Oncology, Biology and Genetics, University of Genova, Genoa, Italy

SOURCE: Anticancer Research (2004), 24(6), 4019-4024
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Solid tumors develop resistance to retinoids during carcinogenesis. One of the strategies to overcome this resistance may include the combination of these mols. with other differentiating, cytotoxic or chromatin-remodelling agents. We analyzed the anti-proliferative activity of two histone-deacetylase inhibitors (HDACIs), Trichostatin A (TSA) and sodium phenylbutyrate (PB), alone or combined with retinoids, all-trans retinoic acid (ATRA) and Ro 41-5253, on two human breast cancer cell lines: the hormone-dependent MCF-7 and the hormone-independent MDA-MB-231. These lines responded differently to retinoids: MCF-7 were sensitive, while MDA-MB-231 were rather resistant. When the retinoids were combined with HDACIs, these mols. potentiated the retinoid activity on growth inhibition, especially for the association Ro 41-5253 and TSA. By FACS anal., we observed that the anti-proliferative effects were only partially due to pro-apoptotic mechanisms, suggesting a cell-cycle block. The efficacy of the retinoids/HDACIs combinations could represent a new strategy in breast cancer chemotherapy, allowing inhibition of both ER+ and ER- cell populations.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 44 CAPLUS

ACCESSION NUMBER: 2004:723785 CAPLUS
DOCUMENT NUMBER: 141:253968

TITLE: Treatment of myelodysplastic syndromes with valproic acid alone or in combination with all-trans retinoic acid

AUTHOR(S): Kuendgen, Andrea; Strupp, Corinna; Aivado, Manuel; Bernhardt, Alf; Hildebrandt, Barbara; Haas, Rainer; Germing, Ulrich; Gattermann, Norbert

CORPORATE SOURCE: Department of Hematology, Oncology, and Clinical Immunology and the Institute of Genetics, Heinrich-Heine-University, Duesseldorf, Germany

SOURCE: Blood (2004), 104(5), 1266-1269
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Valproic acid (VPA) has been shown to inhibit histone deacetylase activity and to synergize with all-trans retinoic acid (ATRA) in the differentiation induction of acute myelogenous leukemia (AML) blasts in vitro. We treated 18 patients with myelodysplastic syndromes (MDS) and AML secondary to MDS (sAML/MDS) with VPA monotherapy (serum concns. 346-693 μM [50-100 μg/mL]). Five patients received VPA and ATRA (80 mg/m2/d, days 1-7, every other week). Response according to international working group (IWG) criteria was observed in 8 patients (44%) on VPA monotherapy, including 1 partial remission. Median response duration was 4 mo (range, 3-9 mo). Four of 5 patients relapsing were treated with VPA + ATRA, 2 of them responding again. Among

5 patients receiving VPA + ATRA from the start, none responded according to IWG criteria, but 1 patient with sAML/MDS achieved a marked reduction in peripheral and marrow blasts. Thus, VPA is of therapeutic benefit for patients with MDS, and ATRA may be effective when added later.

OS.CITING REF COUNT: 107 THERE ARE 107 CAPLUS RECORDS THAT CITE THIS RECORD (108 CITINGS)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:375700 CAPLUS

DOCUMENT NUMBER: 141:360286

TITLE: A quadruple therapy synergistically blocks proliferation and promotes apoptosis of hepatoma cells

AUTHOR(S): Ganslmayer, Marion; Ocker, Matthias; Zopf, Steffen; Leitner, Sandra; Hahn, Eckhart G.; Schuppan, Detlef; Herold, Christoph

CORPORATE SOURCE: Medical Department I, University of Erlangen-Nuernberg, Erlangen, D-91054, Germany

SOURCE: Oncology Reports (2004), 11(5), 943-950
CODEN: OCRPEW; ISSN: 1021-335X

PUBLISHER: Oncology Reports

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Effective therapy for advanced hepatocellular carcinoma (HCC) is lacking. Conventional chemotherapy was judged to be ineffective. We previously demonstrated that the histone deacetylase inhibitor Trichostatin A (TSA) blocks growth of HCC cells in vitro. The anti-tumoral effect of a combination of more than 2 classes of drugs remains unexplored. Four hepatoma cell lines were incubated with increasing concns. of Tamoxifen (TAM), 9-cis retinoic acid (CRA), the methioninaminopeptidase inhibitor TNP-470 and TSA as single agents and in combination. Anti-proliferative and pro-apoptotic effects were assessed using BrdU-incorporation, FACS anal. and immunocytochem. Central pro- and anti-apoptotic proteins were measured by semi-quant. Western blotting and substrate assays. All single substances inhibited proliferation and induced apoptosis in HCC cells only at high concns. The combination of TAM/CRA/TNP/TSA multiplied the anti-tumoral effects, reaching up to 93% inhibition of proliferation and 63% induction of apoptosis after 24 h in Hep1B cells. Pro-apoptotic factors bax and caspase 3 were highly increased with quadruple therapy, while anti-apoptotic bcl-2 decreased to undetectable levels. Fibroblasts remained largely unaffected. While the single substances were not effective on hepatoma cells in tolerable doses, their combination significantly increases anti-tumoral efficacy. Combination therapy with biomodulators is a promising treatment option for HCC.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:268090 CAPLUS

DOCUMENT NUMBER: 140:385630

TITLE: The histone deacetylase inhibitor MS-275 interacts synergistically with fludarabine to induce apoptosis in human leukemia cells

AUTHOR(S): Maggio, Sonia C.; Rosato, Roberto R.; Kramer, Lora B.; Dai, Yun; Rahmani, Mohamed; Paik, David S.; Czarnik, Ann C.; Payne, Shawn G.; Spiegel, Sarah; Grant, Steven

CORPORATE SOURCE: Department of Medicine, Virginia Commonwealth

University/Medical College of Virginia, Richmond, VA, 23298, USA

SOURCE: Cancer Research (2004), 64(7), 2590-2600
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Interactions between the novel benzamide histone deacetylase (HDAC) inhibitor MS-275 and fludarabine were examined in lymphoid and myeloid human leukemia cells in relation to mitochondrial injury, signal transduction events, and apoptosis. Prior exposure of Jurkat lymphoblastic leukemia cells to a marginally toxic concentration of MS-275 (e.g., 500 nM) for 24 h sharply increased mitochondrial injury, caspase activation, and apoptosis in response to a minimally toxic concentration of fludarabine (500 nM), resulting in highly synergistic antileukemic interactions and loss of clonogenic survival. Simultaneous exposure to MS-275 and fludarabine also led to synergistic effects, but these were not as pronounced as observed with sequential treatment. Similar interactions were noted in the case of (a) other human leukemia cell lines (e.g., U937, CCRF-CEM); (b) other HDAC inhibitors (e.g., sodium butyrate); and (c) other nucleoside analogs (e.g., 1-β-D-arabinofuranosylcytosine, gemcitabine). Potentiation of fludarabine lethality by MS-275 was associated with acetylation of histones H3 and H4, down-regulation of the antiapoptotic proteins XIAP and Mcl-1, enhanced cytosolic release of proapoptotic mitochondrial proteins (e.g., cytochrome c, Smac/DIABLO, and apoptosis-inducing factor), and caspase activation. It was also accompanied by the caspase-dependent down-regulation of p27KIP1, cyclins A, E, and D1, and cleavage and diminished phosphorylation of retinoblastoma protein. However, increased lethality of the combination was not associated with enhanced fludarabine triphosphate formation or DNA incorporation and occurred despite a slight reduction in the S-phase fraction. Prior exposure to MS-275 attenuated fludarabine-mediated activation of MEK1/2, extracellular signal-regulated kinase, and Akt, and enhanced c-Jun NH2-terminal kinase phosphorylation; furthermore, inducible expression of constitutively active MEK1/2 or Akt significantly diminished MS-275/fludarabine-induced lethality. Combined exposure of cells to MS-275 and fludarabine was associated with a significant increase in generation of reactive oxygen species; moreover, both the increase in reactive oxygen species and apoptosis were largely attenuated by coadministration of the free radical scavenger L-N-acetylcysteine. Finally, prior administration of MS-275 markedly potentiated fludarabine-mediated generation of the proapoptotic lipid second messenger ceramide. Taken together, these findings indicate that the HDAC inhibitor MS-275 induces multiple perturbations in signal transduction, survival, and cell cycle regulatory pathways that lower the threshold for fludarabine-mediated mitochondrial injury and apoptosis in human leukemia cells. They also provide insights into possible mechanisms by which novel, clin. relevant HDAC inhibitors might be used to enhance the antileukemic activity of established nucleoside analogs such as fludarabine.

OS.CITING REF COUNT: 68 THERE ARE 68 CAPLUS RECORDS THAT CITE THIS RECORD (68 CITINGS)
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:908573 CAPLUS
DOCUMENT NUMBER: 140:192446

TITLE: The proteasome inhibitor bortezomib interacts synergistically with histone deacetylase inhibitors to induce apoptosis in Bcr/Abl+

cells sensitive and resistant to STI571
AUTHOR(S): Yu, Chunrong; Rahmani, Mohamed; Conrad, Daniel; Subler, Mark; Dent, Paul; Grant, Steven
CORPORATE SOURCE: Departments of Medicine, Radiation Oncology, Biochemistry, Microbiology, Human Genetics, and Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA, USA
SOURCE: Blood (2003), 102(10), 3765-3774
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interactions between the proteasome inhibitor bortezomib and histone deacetylase inhibitors (HDIs) have been examined in Bcr/Abl+ human leukemia cells (K562 and LAMA 84). Coexposure of cells (24-48 h) to minimally toxic concns. of bortezomib + either suberoylanilide hydroxamic acid (SAHA) or sodium butyrate (SB) resulted in a striking increase in mitochondrial injury, caspase activation, and apoptosis, reflected by caspases-3 and -8 cleavage and poly(ADP-ribose) polymerase (PARP) degradation These events were accompanied by down-regulation of the Raf-1/mitogen-induced extracellular kinase (MEK)/extracellular signal-related kinase (ERK) pathway as well as diminished expression of Bcr/Abl and cyclin D1, cleavage of p21CIP1 and phosphorylation of the retinoblastoma protein (pRb), and induction of the stress-related kinases Jun kinase (JNK) and p38 mitogen-activated protein kinase (MAPK). Transient transfection of cells with a constitutively active MEK construct significantly protected them from bortezomib/SAHA-mediated lethality. Coadministration of bortezomib and SAHA resulted in increased reactive oxygen species (ROS) generation and diminished nuclear factor κB (NF-κB) activation; moreover, the free radical scavenger L-N-acetylcysteine (LNAC) blocked bortezomib/SAHA-related ROS generation, induction of JNK and p21CIP1, and apoptosis. Lastly, this regimen potently induced apoptosis in STI571 (imatinib mesylate)-resistant K562 cells and CD34+ mononuclear cells obtained from a patient with STI571-resistant disease, as well as in Bcr/Abl- leukemia cells (eg, HL-60, U937, Jurkat). Together, these findings raise the possibility that combined proteasome/histone deacetylase inhibition may represent a novel strategy in leukemia, including apoptosis-resistant Bcr/Abl+ hematol. malignancies.
OS.CITING REF COUNT: 132 THERE ARE 132 CAPLUS RECORDS THAT CITE THIS RECORD (132 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:505874 CAPLUS
DOCUMENT NUMBER: 139:358198
TITLE: Regulation of Retinoic Acid Receptor β Expression by Peroxisome Proliferator-activated Receptor γ Ligands in Cancer Cells
AUTHOR(S): James, Sharon Y.; Lin, Feng; Kolluri, Siva Kumar; Dawson, Marcia I.; Zhang, Xiao-kun
CORPORATE SOURCE: Cancer Center, The Burnham Institute, La Jolla, CA, 92037, USA
SOURCE: Cancer Research (2003), 63(13), 3531-3538
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The peroxisome proliferator-activated receptor γ (PPARγ) is a nuclear receptor family member that can form a heterodimeric complex with retinoid X receptor (RXR) and initiate transcription of target

genes. In this study, we have examined the effects of the PPARγ ligand ciglitazone and the RXR ligand SR11237 on growth and induction of retinoic acid receptor (RAR) β expression in breast and lung cancer cells. Our results demonstrated that ciglitazone and SR11237 cooperatively inhibited the growth of ZR-75-1 and T-47D breast cancer and Calu-6 lung cancer cells. Gel shift anal. indicated that PPARγ, in the presence of RXR, formed a strong complex with a retinoic acid response element (β retinoic acid response element) in the RARβ promoter. In reporter gene assays, RXR ligands and ciglitazone, but not the PPARγ ligand 15d-PGJ2, cooperatively promoted the transcriptional activity of the β retinoic acid response element. Ciglitazone, but not 15d-PGJ2, strongly induced RARβ expression in human breast and lung cancer cell lines when used together with SR11237. The induction of RARβ expression by the ciglitazone and SR11237 combination was diminished by a PPARγ-selective antagonist, bisphenol A diglycidyl ether. All-trans-retinoic acid or the combination of ciglitazone and SR11237 was able to induce RARβ in all-trans- retinoic acid-resistant MDA-MB-231 breast cancer cells only when the orphan receptor chick ovalbumin upstream promoter transcription factor was expressed, or in the presence of the histone deacetylase inhibitor trichostatin A. These studies indicate the existence of a novel RARβ-mediated signaling pathway of PPARγ action, which may provide a mol. basis for developing novel therapies involving RXR and PPARγ ligands in potentiating antitumor responses.

OS.CITING REF COUNT: 35 THERE ARE 35 CAPLUS RECORDS THAT CITE THIS RECORD (35 CITINGS)

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:335539 CAPLUS

DOCUMENT NUMBER: 139:190814

TITLE: Histone Deacetylase Inhibitors Promote STI571-mediated Apoptosis in STI571-sensitive and -resistant Bcr/Abl+ Human Myeloid Leukemia Cells

AUTHOR(S): Yu, Chunrong; Rahmani, Mohamed; Almenara, Jorge; Subler, Mark; Krystal, Geoffrey; Conrad, Daniel; Varticovski, Lubya; Dent, Paul; Grant, Steven

CORPORATE SOURCE: Department of Medicine, Virginia Commonwealth University, Medical College of Virginia, Richmond, VA, 23298, USA

SOURCE: Cancer Research (2003), 63(9), 2118-2126
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Interactions between the Bcr/Abl kinase inhibitor STI571 (Gleevec, imatinib mesylate) and histone deacetylase inhibitors (HDIs) have been examined in STI571-sensitive and -resistant Bcr/Abl+ human leukemia cells (K562 and LAMA 84). Cotreatment of K562 cells with 250 nM imatinib mesylate and 2.0 μM suberoylanilide hydroxamic acid (SAHA) for 24 h, exposures that were minimally toxic alone, resulted in a marked increase in mitochondrial damage (e.g., cytochrome c, Smac/DIABLO, and apoptosis-inducing factor release), caspase activation, and apoptosis. Similar events were observed in other Bcr/Abl+ cells (i.e., LAMA 84), and in cells exposed to STI571 in combination with the HDI sodium butyrate. Coexposure of cells to HDIs in conjunction with STI571 resulted in multiple perturbations in signaling and cell cycle-regulatory proteins, including down-regulation of Raf, phospho-mitogen-activated protein kinase kinase (MEK),

phospho-extracellular signal-regulated kinase (ERK), phospho-Akt, phospho-signal transducers and activators of transcription 5, cyclin D1, and Mcl-1, accompanied by dephosphorylation and cleavage of retinoblastoma protein and a striking increase in phosphorylation of c-Jun NH2-terminal kinase. Coexposure of Bcr/Abl+ cells to STI571 also blocked SAHA-mediated induction of p21CIP1 and resulted in down-regulation of Bcr/Abl protein expression. STI571 and SAHA also interacted synergistically to induce apoptosis in STI571-resistant K562 and LAMA 84 cells that display increased Bcr/Abl protein expression. Lastly, inducible expression of a constitutively active MEK1/2 construct significantly attenuated SAHA/STI571-mediated apoptosis in K562 cells, implicating disruption of the Raf/MEK/ERK axis in synergistic antileukemic effects of this drug combination. Together, these findings indicate that combined exposure of Bcr/Abl+ cells to the kinase inhibitor STI571 and HDIs leads to diverse perturbations in signaling and cell cycle-regulatory proteins, associated with a marked increase in mitochondrial damage and cell death. They also raise the possibility that this strategy may be effective in some Bcr/Abl+ cells that are resistant to STI571 through increased Bcr/Abl expression.

OS.CITING REF COUNT: 81 THERE ARE 81 CAPLUS RECORDS THAT CITE THIS RECORD (81 CITINGS)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:594666 CAPLUS

DOCUMENT NUMBER: 137:135074

TITLE: Use of retinoids plus histone deacetylase inhibitors to inhibit the growth of solid tumors

INVENTOR(S): Gudas, Lorraine J.; Nanus, David

PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA

SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002060430	A1	20020808	WO 2002-US2976		20020201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002242057	A1	20020812	AU 2002-242057		20020201
US 20020183388	A1	20021205	US 2002-61101		20020201
PRIORITY APPLN. INFO.:			US 2001-265651P	P	20010201
			WO 2002-US2976	W	20020201

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides a method of inhibiting growth of solid tumors in an animal which comprises administering an effective amount of trichostatin A to an animal in need of such treatment. The invention also provides a method of inhibiting growth of solid tumors in an animal which comprises administering an effective amount of a histone deacetylase inhibitor and a retinoid to an

animal in need of such treatment. Examples of solid tumors which may be treated using the methods of the invention include but are not limited to carcinomas of the head and neck, breast, skin, kidney, oral cavity, colon, prostate, pancreas and lung.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:131947 CAPLUS

DOCUMENT NUMBER: 136:161019

TITLE: Frequent mutations in the ligand-binding domain of PML-RARα after multiple relapses of acute promyelocytic leukemia: analysis for functional relationship to response to all-trans retinoic acid and histone deacetylase inhibitors in vitro and in vivo

AUTHOR(S): Zhou, Da-Cheng; Kim, Soon H.; Ding, Wei; Schultz, Cynthia; Warrell, Raymond P., Jr.; Gallagher, Robert E.

CORPORATE SOURCE: Departments of Oncology and Pathology, Montefiore Medical Center, Albert Einstein Cancer Center, Bronx, NY, 10467, USA

SOURCE: Blood (2002), 99(4), 1356-1363
CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study identified missense mutations in the ligand binding domain of the oncoprotein PML-RARα in 5 of 8 patients with acute promyelocytic leukemia (APL) with 2 or more relapses and 2 or more previous courses of all-trans retinoic acid (RA)-containing therapy. Four mutations were novel (Lys207Asn, Gly289Arg, Arg294Trp, and Pro407Ser), whereas one had been previously identified (Arg272Gln; normal RARα1 codon assignment). Five patients were treated with repeat RA plus phenylbutyrate (PB), a histone deacetylase inhibitor, and one patient experienced a prolonged clin. remission. Of the 5 RA + PB-treated patients, 4 had PML-RARα mutations. The Gly289Arg mutation in the clin. responder produced the most defective PML-RARα function in the presence of RA with or without sodium butyrate (NaB) or trichostatin A. Relapse APL cells from this patient failed to differentiate in response to RA but partially differentiated in response to NaB alone, which was augmented by RA. In contrast, NaB alone had no differentiation effect on APL cells from another mutant case (Pro407Ser) but enhanced differentiation induced by RA. These results indicate that PML-RARα mutations occurred with high frequency after multiple RA treatment relapses, indicate that the functional potential of PML-RARα was not correlated with clin. response to RA + PB treatment, and suggest that the response to RA + PB therapy in one patient was related to the ability of PB to circumvent the blocked RA-regulated gene response pathway.

OS.CITING REF COUNT: 63 THERE ARE 63 CAPLUS RECORDS THAT CITE THIS RECORD (63 CITINGS)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:869449 CAPLUS

DOCUMENT NUMBER: 136:336100

TITLE: Silencing mediator of retinoid and thyroid hormone receptors and activating signal cointegrator-2

as transcriptional coregulators of the orphan nuclear receptor Nur77

AUTHOR(S): Sohn, Young Chang; Kwak, Eunyee; Na, Yeonja; Lee, Jae Woon; Lee, Soo-Kyung

CORPORATE SOURCE: Department of Life Science, Pohang University of Science and Technology, Pohang, 790-784, S. Korea

SOURCE: Journal of Biological Chemistry (2001), 276(47), 43734-43739
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB For the orphan nuclear receptor subfamily that includes Nur77 (NGFI-B), Nurr1, and NOR-1, no transcriptional coregulators have been identified thus far. In this report, we found that Ca2+/calmodulin-dependent protein kinase IV enhances Nur77 transactivation in cotransfections either alone or in synergy with AF2-dependent coactivator ASC-2, whereas corepressor silencing mediator for retinoid and thyroid hormone receptors (SMRT) is repressive. Interestingly, Nur77 interacted with SMRT but did not directly bind ASC-2, and accordingly, the putative AF2 core domain of Nur77 did not affect the Nur77 transactivation. SMRT harbors transferable repression domains that associate with various histone deacetylases. Surprisingly, histone deacetylase inhibitor trichostatin A was unable to block the repressive effect of SMRT while dramatically stimulating the Nur77 transactivation. These results suggest that SMRT and ASC-2 are specific coregulators of Nur77 and that SMRT may dynamically compete with a putative adaptor mol., which links ASC-2 to Nur77, for the identical binding sites within Nur77 in vivo.

OS.CITING REF COUNT: 26 THERE ARE 26 CAPLUS RECORDS THAT CITE THIS RECORD (26 CITINGS)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:503786 CAPLUS

DOCUMENT NUMBER: 135:298293

TITLE: In vivo effects of a histone deacetylase inhibitor, FK228, on human acute promyelocytic leukemia in NOD/Shi-scid/scid mice

AUTHOR(S): Kosugi, Hiroshi; Ito, Masafumi; Yamamoto, Yukiya; Towatari, Masayuki; Ito, Mamoru; Ueda, Ryuzo; Saito, Hidehiko; Naoe, Tomoki

CORPORATE SOURCE: First Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, 466-8560, Japan

SOURCE: Japanese Journal of Cancer Research (2001), 92(5), 529-536
CODEN: JJCREP; ISSN: 0910-5050

PUBLISHER: Japanese Cancer Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Histone acetylation and deacetylation are closely linked to transcriptional activation and repression, resp. In acute promyelocytic leukemia (APL), histone deacetylase inhibitors (HDACIs) have a synergistic effect with all-trans retinoic acid (ATRA) in vitro to induce differentiation. Here we report in vitro and in vivo effects of a HDACI, FK228 (formerly FR901228 or depsipeptide), on the human APL cell line NB4. FK228 had a strong and irreversible cytotoxicity compared with another HDACI, trichostatin A. In vivo administration of ATRA or FK228 alone partly inhibited the growth of

established tumors of NB4 s.c. transplanted in NOD/Shi-scid/scid mice, and the combination was synergistically effective. Histopathol. examination revealed that the combination induced apoptosis and differentiation as well as histone acetylation. I.V. injection of NB4 in NOD/Shi-scid/scid mice followed by combination treatment significantly prevented leukemia death, whereas single administration did not. These findings suggest that FK228 is a promising agent to enhance ATRA-sensitivity in the treatment of APL.

OS.CITING REF COUNT: 40 THERE ARE 40 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:501130 CAPLUS

DOCUMENT NUMBER: 135:191912

TITLE: SMRTe inhibits MEF2C transcriptional activation by targeting HDAC4 and 5 to nuclear domains

AUTHOR(S): Wu, Xiaoyang; Li, Hui; Park, Eun-Ju; Chen, J. Don

CORPORATE SOURCE: Department of Biochemistry and Molecular Pharmacology, University of Massachusetts Medical School, Worcester, MA, 01655, USA

SOURCE: Journal of Biological Chemistry (2001), 276(26), 24177-24185
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The silencing mediator for retinoic acid and thyroid hormone receptors (SMRT) mediates transcriptional repression by recruiting histone deacetylases (HDACs) to the DNA-bound nuclear receptor complex. The full-length SMRT (SMRTe) contains an N-terminal sequence that is highly conserved to the nuclear receptor corepressor N-CoR. To date, little is known about the activity and function of the full-length SMRTe protein, despite extensive studies on separated receptor interaction and transcriptional repression domains. Here we show that SMRTe inhibits MEF2C transcriptional activation by targeting selective HDACs to unique subnuclear domains. Indirect immunofluorescence studies with anti-SMRTe antibody reveal discrete cytoplasmic and nuclear speckles, which contain RARα in an RA-sensitive manner. Formation of the SMRTe nuclear speckles results in recruitment of several class I and class II HDACs to these subnuclear domains in a process depending on HDAC enzymic activity. Intriguingly, although HDAC4 is located primarily in the cytoplasm, coexpression of SMRTe dramatically translocates HDAC4 from the cytoplasm into the nucleus, where HDAC4 prevents MEF2C from activating muscle differentiation. SMRTe also translocates HDAC5 from diffusive nucleoplasm into discrete nuclear domains. Accordingly, SMRTe synergizes with HDAC4 and 5 to inhibit MEF2C transactivation of target promoter, suggesting that nuclear domain targeting of HDAC4/5 may be important in preventing muscle cell differentiation. These results highlight an unexpected new function of the nuclear receptor corepressor SMRTe for its role in regulating cellular trafficking of nuclear receptor and selective HDACs that may play an important role in regulation of cell growth and differentiation.

OS.CITING REF COUNT: 40 THERE ARE 40 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:495131 CAPLUS

DOCUMENT NUMBER: 136:318891
TITLE: Antineoplastic action of 5-aza-2'-deoxycytidine and histone deacetylase inhibitor and their effect on the expression of retinoic acid receptor β and estrogen receptor α genes in breast carcinoma cells
AUTHOR(S): Bovenzi, Veronica; Momparler, Richard L.
CORPORATE SOURCE: Departement de pharmacologie, Universite de Montreal, Quebec, Can.
SOURCE: Cancer Chemotherapy and Pharmacology (2001), 48(1), 71-76
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During tumorigenesis several cancer-related genes can be silenced by aberrant methylation. In many cases these silenced genes can be reactivated by exposure to the DNA methylation inhibitor, 5-aza-2'-deoxycytidine (5-AZA-CdR). Histone acetylation also plays a role in the control of expression of some genes. The aim of this study was to determine the antineoplastic activities of 5-AZA-CdR and trichostatin A (TSA), either administered alone or in combination, in MDA-MB-231 breast carcinoma cells. The effects of these drugs (alone and in combination) on the expression of the tumor suppressor gene, retinoic acid receptor (RARβ) and of the estrogen receptor α gene (ERα), whose expression is lost in the cell line used in the study, were also investigated. MDA-MB-231 cells were treated with 5-AZA-CdR and TSA and the antitumor activity of these drugs was determined by clonogenic assay. Total RNA was extracted from the treated cells and RT-PCR was used to determine the effect of the treatment on the expression of RARβ and ERα. Methylation-sensitive PCR anal. was used to confirm that lack of expression of both genes was due to hypermethylation of their promoter regions. A single nucleotide primer extension assay was also used to quantify the reduction in DNA methylation following drug treatment. Both 5-AZA-CdR and TSA alone showed significant antineoplastic activity. The combination of the two drugs was synergistic with respect to MDA-MB-231 cell kill. 5-AZA-CdR alone weakly activated the expression of both RARβ and ERα. TSA alone only activated RARβ, but not ERα. The combination of these agents appeared to produce a greater activation of both genes. Thus, the interesting interaction between 5-AZA-CdR and TSA in both cell kill and cancer-related gene reactivation provides a rationale for the use of inhibitors of DNA methylation and histone deacetylation in combination for the chemotherapy of breast cancer.

OS.CITING REF COUNT: 69 THERE ARE 69 CAPLUS RECORDS THAT CITE THIS RECORD (69 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:354366 CAPLUS
DOCUMENT NUMBER: 135:146992
TITLE: The histone deacetylase inhibitor, CBHA, inhibits growth of human neuroblastoma xenografts in vivo, alone and synergistically with all-trans retinoic acid
AUTHOR(S): Coffey, Dennis C.; Kutko, Martha C.; Glick, Richard D.; Butler, Lisa M.; Heller, Glenn; Rifkind, Richard A.; Marks, Paul A.; Richon, Victoria M.; La Quaglia, Michael P.

CORPORATE SOURCE: Department of Pediatrics, Sloan-Kettering Institute and Memorial Sloan-Kettering Cancer Center, Joan and Sanford I. Weill Graduate School of Medical Sciences of Cornell University, New York, NY, 10021, USA
SOURCE: Cancer Research (2001), 61(9), 3591-3594
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Histone deacetylase inhibitors (HDACIs) inhibit the growth of a variety of transformed cells in culture. We demonstrated previously that the hybrid-polar HDACI m-carboxycinnamic acid bis-hydroxamide (CBHA) induces apoptosis of human neuroblastoma in vitro and is effective in lower doses when combined with retinoids . The current study investigates the effect of CBHA on the growth of human neuroblastoma in vivo, both alone and in combination with all-trans retinoic acid (atRA), using a severe combined immunodeficiency-mouse xenograft model. CBHA (50, 100, and 200 mg/kg/day) inhibited growth of SMS-KCN-69n tumor xenografts in a dose-dependent fashion, with 200 mg/kg CBHA resulting in a complete suppression of tumor growth. The efficacy of 50 and 100 mg/kg CBHA was enhanced by the addition of 2.5 mg/kg atRA. This dose of atRA was ineffective when administered alone. Treatment was accompanied by mild weight loss in all groups except the lowest dose of CBHA. Our results suggest HDACIs alone or combined with retinoids may have therapeutic utility for neuroblastoma.
OS.CITING REF COUNT: 83 THERE ARE 83 CAPLUS RECORDS THAT CITE THIS RECORD (83 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:44192 CAPLUS
DOCUMENT NUMBER: 134:260995
TITLE: Effects of retinoic acid and sodium butyrate on gene expression, histone acetylation and inhibition of proliferation of melanoma cells
AUTHOR(S): Demary, K.; Wong, L.; Spanjaard, R. A.
CORPORATE SOURCE: Department of Otolaryngology, Boston University School of Medicine, Cancer Research Center, Boston, MA, 02118, USA
SOURCE: Cancer Letters (Shannon, Ireland) (2001), 163(1), 103-108
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retinoic acid (RA) induces growth-arrest of many tumor cell lines but it is an ineffective therapeutic against melanoma. We investigated whether the histone deacetylase (HDAC)-inhibitor sodium butyrate (BUT) can restore or potentiate the RA-response of RA-resistant human A375, and RA-responsive S91 murine melanoma cells. BUT induced expression of RARβ and p21waf1/cip1 mRNA in A375 cells but in S91 cells only p21waf1/cip1 was induced. RA and BUT synergistically activated transcription of an RA-dependent reporter gene in S91, but not A375 cells. BUT increased histone H4 acetylation in both cell types. RA potentiated BUT-mediated inhibition of S91 cell proliferation, whereas A375 cells remained largely resistant to both compds. HDAC-inhibitors may enhance the activity of RA on RA-responsive melanoma cells.
OS.CITING REF COUNT: 38 THERE ARE 38 CAPLUS RECORDS THAT CITE THIS RECORD (38 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:738284 CAPLUS
DOCUMENT NUMBER: 134:304809
TITLE: New drugs for the treatment of chronic lymphocytic leukemia
AUTHOR(S): Cheson, Bruce D.; Dancey, Janet; Murgo, Anthony
CORPORATE SOURCE: Cancer Therapy Evaluation Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Reviews in Clinical and Experimental Hematology (2000), 4(2), 145-166
CODEN: RCEHFB; ISSN: 1127-0020
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 141 refs. Novel strategies are needed to improve the prognosis of patients with chronic lymphocytic leukemia (CLL). One approach is to identify new drugs with unique mechanisms of action. Compound GW506U78, the prodrug for arabinosylguanine, is an interesting new purine analog, which induces responses in about one-third of patients with relapsed or refractory CLL. A multicenter study is currently evaluating patients with CLL who have failed treatment with both fludarabine and an alkylating agent. Other agents in clin. development include retinoids and arsenicals which induce apoptosis, farnesyl transferase inhibitors, proteasome inhibitors and the signal transduction modulators, bryostatin and UCN-01. UCN-01 not only inhibits protein kinase C, but also modulates the G2 checkpoint. In vitro synergy has been demonstrated with fludarabine and a phase I trial of this combination is ongoing at the National Cancer Institute, USA. Flavopiridol is a semisynthetic flavone derivative which is active against cycling as well as noncycling cells. It inhibits a variety of cyclins and induces apoptosis. The histone deacetylase inhibitor depsipeptide has selective activity against CLL cells in vitro. An increasing body of evidence has implicated angiogenesis in hematol. malignancies, such as multiple myeloma, lymphoma and CLL. Several angiogenesis inhibitors are currently in clin. trials, including thalidomide, SU5416 and SU6668. Future strategies must be directed at appropriate therapeutic targets using rational combinations of these drugs and other new compds. with the goal of curing patients with CLL.
REFERENCE COUNT: 141 THERE ARE 141 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:148677 CAPLUS
DOCUMENT NUMBER: 132:274003
TITLE: Sodium butyrate/retinoic acid costimulation induces apoptosis-independent growth arrest and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid
AUTHOR(S): Buommino, E.; Pasquali, D.; Sinisi, A. A.; Bellastella, A.; Morelli, F.; Metafora, S.
CORPORATE SOURCE: CNR International Institute of Genetics and Biophysics, Naples, Italy
SOURCE: Journal of Molecular Endocrinology (2000), 24(1), 83-94
CODEN: JMLEEI; ISSN: 0952-5041
PUBLISHER: Society for Endocrinology

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retinoic acid (RA) and sodium butyrate (NaB) are regulators of cell growth and differentiation. We studied their effect on normal (SVC1) or v-Ki-ras-transformed (Ki-SVC1) rat seminal vesicle (SV) epithelial cell lines. The treatment of these cells with 10-7 M RA did not produce significant changes in the morphol. and biochem. parameters analyzed. When RA was used in combination with 2 mM NaB, the treatment induced substantial morphol. changes, apoptosis-independent growth arrest, up-regulation of tissue transglutaminase (tTGase), and down-regulation of β and γ RA receptor (RAR) mRNA expression. The same cells did not express RAR α either before or after NaB/RA treatment. A similar treatment did not change the amount of mRNA coding for the protein SV-IV (a typical differentiation marker of the SV epithelium) in normal or ras-transformed cells nor the level of v-Ki-ras mRNA in Ki-SVC1 cells. These findings suggest that a defective RA/RARs signaling pathway is probably the biochem. condition that underlies the unresponsiveness to RA of our in vitro culture system, and indirectly points to the possibility that the NaB/RA-induced effects were brought about by a cooperation at the transcription level between the histone deacetylase inhibitory activity of NaB and the ability of RA/RAR to modulate the expression of various genes involved in the control of cell growth and differentiation.
OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:125583 CAPLUS
DOCUMENT NUMBER: 132:263351
TITLE: Drg-1 as a differentiation-related, putative metastatic suppressor gene in human colon cancer
AUTHOR(S): Guan, Rong J.; Ford, Heide L.; Fu, Yineng; Li, Youzhi; Shaw, Leslie M.; Pardee, Arthur B.
CORPORATE SOURCE: Division of Gastroenterology, Brigham and Women's Hospital Beth Israel-Deaconess Medical Center, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Cancer Research (2000), 60(3), 749-755
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A gene related to cell differentiation was identified by differential display as a candidate suppressor of metastases in colon cancer. This gene, with a full-length cDNA of 3 kb, is expressed in normal colon and primary colon cancer tissues and cell lines but not in their metastatic counterparts. A GenBank search found that it is identical to a recently cloned gene, differentiation-related gene-1 (Drg-1), isolated from differentiated HT-29 colon cancer cells. Stable transfection of the SW620 metastatic colon cancer cell line with Drg-1 cDNA induced morphol. changes consistent with differentiation and up-regulated the expression of several colonic epithelial cell differentiation markers (alkaline phosphatase, carcinoembryonic antigen, and E-cadherin). Moreover, the expression of Drg-1 is controlled by several known cell differentiation reagents, such as ligands of peroxisome proliferator-activated receptor γ (troglitazone and BRL46593) and of retinoid X receptor (LG268), and histone deacetylase inhibitors (trichostatin A, suberoylanilide hydroxamic acid, and tributyrin). A synergistic induction of Drg-1 expression was seen with the combination of tributyrin and a low dose of 5'-aza-2'-deoxycytidine (100 nM), an inhibitor of DNA methylation. Functional studies revealed that

overexpression of Drg-1 in metastatic colon cancer cells reduced in vitro invasion through Matrigel and suppressed in vivo liver metastases in nude mice. We propose that Drg-1 suppresses colon cancer metastasis by inducing colon cancer cell differentiation and partially reversing the metastatic phenotype.

OS.CITING REF COUNT: 131 THERE ARE 131 CAPLUS RECORDS THAT CITE THIS RECORD (131 CITINGS)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:655736 CAPLUS

DOCUMENT NUMBER: 132:131906

TITLE: Histone deacetylase inhibitors are the potent inducer/enhancer of differentiation in acute myeloid leukemia: a new approach to anti-leukemia therapy

AUTHOR(S): Kosugi, H.; Towatari, M.; Hatano, S.; Kitamura, K.; Kiyoi, H.; Kinoshita, T.; Tanimoto, M.; Murate, T.; Kawashima, K.; Saito, H.; Naoe, T.

CORPORATE SOURCE: First Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, 466-8550, Japan

SOURCE: Leukemia (1999), 13(9), 1316-1324
CODEN: LEUKED; ISSN: 0887-6924

PUBLISHER: Stockton Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors investigated the effect of the histone deacetylase inhibitors (HDIs), trichostatin A (TSA) and trapoxin A on leukemia cells and cell lines from the viewpoint of differentiation induction. TSA induced differentiation in erythroid cell lines by itself, whereas it synergistically enhanced the differentiation that was directed by all-trans retinoic acid (ATRA) or vitamin D3 in U937, HL60 and NB4 cells. The combined treatment of HDI with ATRA induced differentiation in ATRA-resistant HL60 and NB4 cells. The transcriptional expression during the treatment with HDI was examined in HL60, U937 and MEG-01. Cell cycle-regulator genes (p21waf1 and p16INK4A) were upregulated or constantly expressed, erythroid-specific genes (GATA-1, β-globin) were silent or downregulated, and housekeeping genes (β-actin and GAPDH) were constantly expressed. Twelve of 35 (34%) clin. samples from acute myeloid leukemia patients ranging from M0 to M7 also displayed both phenotypical and morphol. changes by the treatment with TSA alone. HDIs are thus the potent inducer or enhancer of differentiation in acute myeloid leukemia and regulate transcription in an ordered manner.

OS.CITING REF COUNT: 101 THERE ARE 101 CAPLUS RECORDS THAT CITE THIS RECORD (101 CITINGS)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:483377 CAPLUS

DOCUMENT NUMBER: 131:125449

TITLE: Transcription therapy for cancers using a retinoic acid and/or an inhibitor of histone deacetylase

INVENTOR(S): Pandolfi, Pier Paolo; Warrell, Raymond P., Jr.; Zelent, Arthur

PATENT ASSIGNEE(S): Sloan Kettering Institute for Cancer Research, USA

SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9937150	A1	19990729	WO 1999-US1212		19990120
W: CA, JP					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 6262116	B1	20010717	US 1998-154672		19980918
PRIORITY APPLN. INFO.:			US 1998-72279P	P	19980123
			US 1998-154672	A	19980918

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention provides a method of treating a neoplastic condition in an individual, comprising administering a pharmacol. ED of a retinoic acid and/or an inhibitor of histone deacetylase. Also provided is a pharmaceutical composition comprising a retinoic acid, an inhibitor of histone deacetylase, and a pharmaceutically acceptable carrier. Further provided is a method of inducing terminal differentiation of tumor cells in a tumor in an individual in need of such treatment, comprising the step of administering a pharmacol. ED of a retinoic acid and/or an inhibitor of histone deacetylase.

OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:325757 CAPLUS
DOCUMENT NUMBER: 130:332877
TITLE: Methods for the use of inhibitors of co-repressors for the treatment of neoplastic diseases
INVENTOR(S): Evans, Ronald M.; Lin, Richard J.; Nagy, Laszlo
PATENT ASSIGNEE(S): The Salk Institute for Biological Studies, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9923885	A1	19990520	WO 1998-US23962		19981110
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6706762	B1	20040316	US 1997-966876		19971110
CA 2308377	A1	19990520	CA 1998-2308377		19981110
AU 9913959	A	19990531	AU 1999-13959		19981110
EP 1037533	A1	20000927	EP 1998-957781		19981110
R: CH, DE, FR, GB, LI					
PRIORITY APPLN. INFO.:			US 1997-966876	A2	19971110
			US 1997-846881	A2	19970501
			WO 1998-US23962	W	19981110

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention is related to the use of histone deacetylase inhibitors as activators of genes responsive to hormone receptors and to counteract the oncogenic functions of oncogenic proteins. Histone deacetylase relieves repressed systems and, when in combination with a ligand for a member of the steroid/thyroid hormone superfamily, the differentiation effects of retinoids are enhanced. Formulations for modulating hormone-mediated processes and assays for the identification of potential modulators are presented.

OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:672958 CAPLUS

DOCUMENT NUMBER: 127:342180

ORIGINAL REFERENCE NO.: 127:67055a,67058a

TITLE: A histone deacetylase inhibitor potentiates retinoid receptor action in embryonal carcinoma cells

AUTHOR(S): Minucci, Saverio; Horn, Valerie; Bhattacharyya, Nisan; Russanova, Valya; Ogryzko, Vasily V.; Gabriele, Lucia; Howard, Bruce H.; Ozato, Keiko

CORPORATE SOURCE: Lab. Mol. Growth Regulation, Natl. Inst. Child Health Human Dev., Natl. Inst. Health, Bethesda, MD, 20892, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(21), 11295-11300 CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Histone acetylation is thought to have a role in transcription. To gain insight into the role of histone acetylation in retinoid -dependent transcription, we studied the effects of trichostatin A (TSA), a specific inhibitor of histone deacetylase, on P19 embryonal carcinoma cells. We show that coaddn. of TSA and retinoic acid (RA) markedly enhances neuronal differentiation in these cells, although TSA alone does not induce differentiation but causes extensive apoptosis. Consistent with the cooperative effect of TSA and RA, coaddn. of the two agents synergistically enhanced transcription from stably integrated RA-responsive promoters. The transcriptional synergy by TSA and RA required the RA-responsive element and a functional retinoid X receptor (RXR)/ retinoic acid receptor (RAR) heterodimer, both obligatory for RA-dependent transcription. Furthermore, TSA led to promoter activation by an RXR-selective ligand that was otherwise inactive in transcription. In addition, TSA enhanced transcription from a min. basal promoter, independently of the RA-responsive element. Finally, we show that TSA alone or in combination with RA increases in vivo endonuclease sensitivity within the RA-responsive promoter, suggesting that TSA treatment might alter a local chromatin environment to enhance RXR/RAR heterodimer action. Thus, these results indicate that histone acetylation influences activity of the heterodimer, which is in line with the observed interaction between the RXR/RAR heterodimer and a histone acetylase presented elsewhere.

OS.CITING REF COUNT: 78 THERE ARE 78 CAPLUS RECORDS THAT CITE THIS RECORD (78 CITINGS)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 44 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:311610 CAPLUS
DOCUMENT NUMBER: 127:31908
ORIGINAL REFERENCE NO.: 127:6109a,6112a
TITLE: Nuclear receptor repression mediated by a complex containing SMRT, mSin3A, and histone deacetylase
AUTHOR(S): Nagy, Laszlo; Kao, Hung-Ying; Chakravarti, Debabrata; Lin, Richard J.; Hassig, Christian A.; Ayer, Donald E.; Schreiber, Stuart L.; Evans, Ronald M.
CORPORATE SOURCE: Salk Inst. Biological Studies, Howard Hughes Med. Inst., La Jolla, CA, 92037, USA
SOURCE: Cell (Cambridge, Massachusetts) (1997), 89(3), 373-380
CODEN: CELLB5; ISSN: 0092-8674
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The transcriptional corepressors SMRT and N-CoR function as silencing mediators for retinoid and thyroid hormone receptors. Here, we show that SMRT and N-Cor directly interact with mSin3A, a corepressor for the Mad-Max heterodimer and a homolog of the yeast global-transcriptional repressor Sin3p. In addition, we demonstrate that the recently characterized histone deacetylase 1 (HDAC1) interacts with Sin3A and SMRT to form a multisubunit repressor complex. Consistent with this model, we find that HDAC inhibitors synergize with retinoic acid to stimulate hormone-responsive genes and differentiation of myeloid leukemia (HL-60) cells. This work establishes a convergence of repression pathways for bHLH-Zip proteins and nuclear receptors and suggests this type of regulation may be more widely conserved than previously suspected.
OS.CITING REF COUNT: 902 THERE ARE 902 CAPLUS RECORDS THAT CITE THIS RECORD (902 CITINGS)
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2004387274 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15291362
TITLE: Granulocytic differentiation of leukemic cells with t(9;11)(p22;q23) induced by all-trans-retinoic acid.
AUTHOR: Iijima Kimiko; Honma Yoshio; Niitsu Nozomi
CORPORATE SOURCE: First Department of Internal Medicine, Toho University School of Medicine, Tokyo, Japan.
SOURCE: Leukemia & lymphoma, (2004 May) Vol. 45, No. 5, pp. 1017-24.
Journal code: 9007422. ISSN: 1042-8194.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 5 Aug 2004
Last Updated on STN: 31 Dec 2004
Entered Medline: 30 Dec 2004
AB Acute leukemia patients with MLL (mixed linage leukemia) rearrangements tend to respond poorly to conventional therapies. We examined differentiation of human myeloid leukemia cells displaying the MLL-AF9 gene, using several differentiation agents. When MOLM-14 cells were treated with all-trans retinoic acid (ATRA) or 1beta,25-dihydroxyvitamin D3, significant induced differentiation was observed. Trichostatin A (TSA), an inhibitor of histone deacetylase, demonstrated enhance effects with ATRA in regard to growth inhibition and differentiation induction in MOLM-14 cells. Pretreatment with TSA before exposure to ATRA displayed increased

effect. Based on these findings, combined treatment with ATRA and TSA may be clinically useful in therapy for acute leukemia displaying MLL-AF9 fusion gene.

L3 ANSWER 26 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2004010421 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14707268
TITLE: Simultaneous activation of the intrinsic and extrinsic pathways by histone deacetylase (HDAC) inhibitors and tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) synergistically induces mitochondrial damage and apoptosis in human leukemia cells.
AUTHOR: Rosato Roberto R; Almenara Jorge A; Dai Yun; Grant Steven
CORPORATE SOURCE: Department of Medicine, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298, USA.
CONTRACT NUMBER: CA63753 (United States NCI NIH HHS)
CA83705 (United States NCI NIH HHS)
CA93738 (United States NCI NIH HHS)
SOURCE: Molecular cancer therapeutics, (2003 Dec) Vol. 2, No. 12, pp. 1273-84.
Journal code: 101132535. ISSN: 1535-7163.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 7 Jan 2004
Last Updated on STN: 17 Sep 2004
Entered Medline: 16 Sep 2004
AB Interactions between histone deacetylase (HDAC) inhibitors and tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), also known as Apo2 ligand, were examined in human leukemia cells (e.g., U937, Jurkat, and HL-60). Simultaneous exposure of cells to 100-ng/ml TRAIL with either 1-mM sodium butyrate or 2- micro M suberoylanilide hydroxamic acid resulted in a striking increase in leukemic cell mitochondrial damage, caspase activation, and apoptosis. Lethal effects were significantly diminished in U937 cells ectopically expressing dominant-negative caspase-8, dominant-negative Fas-associated death domain, CrmA (receptor pathway), or Bcl-2 or Bcl-X(L) (mitochondrial pathway). Analysis of mitochondrial events in U937 cells exposed to TRAIL/HDAC inhibitors revealed enhanced Bid activation and Bax translocation, loss of mitochondrial membrane potential, and cytoplasmic release of cytochrome c, Smac/DIABLO, and apoptosis-inducing factor. No changes were observed in expression of FLICE-like inhibitory protein, TRAIL receptors, or reactive oxygen species generation. TRAIL/HDAC inhibitor-induced apoptosis triggered caspase-dependent cleavage of p21(WAF1/CIP1); moreover, enforced expression of a nuclear localization signal deletant form of p21(WAF1/CIP1) significantly diminished lethality. Lastly, p27(KIP1), pRb, X-linked inhibitor of apoptosis, and Bcl-2 displayed extensive proteolysis. These findings indicate that coadministration of TRAIL with HDAC inhibitors synergistically induces apoptosis in human myeloid leukemia cells and provide further evidence that simultaneous activation of the extrinsic and intrinsic pathways in such cells leads to a dramatic increase in mitochondrial injury and activation of the caspase cascade.

L3 ANSWER 27 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2001455354 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11501579

TITLE: Epigenetic downregulation of the retinoic acid receptor-beta2 gene in breast cancer.
AUTHOR: Widschwendter M; Berger J; Muller H M; Zeimet A G; Marth C
CORPORATE SOURCE: Department of Obstetrics and Gynecology, University of Innsbruck, Austria.. martin.widschwendter@uklibk.ac.at
SOURCE: Journal of mammary gland biology and neoplasia, (2001 Apr) Vol. 6, No. 2, pp. 193-201. Ref: 68
Journal code: 9601804. ISSN: 1083-3021.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 15 Aug 2001
Last Updated on STN: 22 Jan 2002
Entered Medline: 20 Dec 2001

AB A growing body of evidence supports the hypothesis that the retinoic acid receptor beta2 (RAR-beta2) gene is a tumor suppressor gene which induces apoptosis and that the chemopreventive and therapeutic effects of retinoids are due to induction of RAR-beta2. During breast cancer progression, RAR-beta2 is reduced or even lost. It is known from studies of other tumor-suppressor genes that methylation of the 5'-region is the cause of loss of expression. Several groups demonstrated that this is also true for the RAR-beta2 in breast cancer by treating breast cancer cell lines with a demethylating agent and examining expression of the RAR-beta2 gene in response to a challenge with retinoic acid. Studies using sodium bisulfite genomic sequencing as well as methylation specific PCR showed that a number of breast cancer cell lines as well as breast cancer tissue showed signs of methylation. The RAR-beta2 gene was unmethylated in non-neoplastic breast tissue as well as in other normal tissues. A combination of retinoic acid with demethylating agents as well as with histone deacetylase inhibitors acts synergistically to inhibit growth. This review presents data that suggest that treatment of cancer patients with demethylating agents followed by retinoic acid may offer a new therapeutic modality. Both the time of commencement of chemoprevention and the choice of substances that are able either to prevent de novo methylation or to reverse methylation-caused gene silencing may be important considerations.

L3 ANSWER 28 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2001110443 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11107121
TITLE: Histone deacetylase inhibitors and retinoic acids inhibit growth of human neuroblastoma in vitro.
AUTHOR: Coffey D C; Kutko M C; Glick R D; Swendeman S L; Butler L; Rifkind R; Marks P A; Richon V M; LaQuaglia M P
CORPORATE SOURCE: Department of Pediatrics, Sloan-Kettering Institute and Memorial Sloan-Kettering Cancer Center, New York, New York 10021, USA.
SOURCE: Medical and pediatric oncology, (2000 Dec) Vol. 35, No. 6, pp. 577-81.
Journal code: 7506654. ISSN: 0098-1532.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001

Last Updated on STN: 22 Mar 2001
Entered Medline: 2 Feb 2001

AB BACKGROUND: Neuroblastoma is a common childhood cancer with a poor overall prognosis. Retinoic acids (RAs) have been studied as a potential therapy, showing promise in recurrent disease. The histone deacetylase inhibitor (HDACI) M-carboxycinnamic acid bishydroxamide (CBHA) is another potential therapy, which we recently described. Combinations of RAs and HDACIs currently under investigation display synergy in certain neoplasms. In this study, we evaluate the effect of combinations of RAs and HDACIs on human neuroblastoma cells. PROCEDURE: Established cell lines were cultured in increasing concentrations of HDACIs, RAs, and combinations thereof. Following exposure, viable cell number was quantified by trypan blue dye exclusion on a hemacytometer. Cell cycle analysis was performed by propidium iodide staining and FACS. RESULTS: All assayed HDACIs and RAs decreased viable cell number. Lower concentrations of each agent were effective when the two were combined. The primary reason for decreased cell number appears to be apoptosis following HDACI exposure and G1 arrest following RA exposure. Both effects are seen with cotreatment. Caspase inhibition abrogates the apoptotic response. CONCLUSIONS: CBHA causes apoptosis of human neuroblastoma in vitro, an effect that can add to the effects of RA. HDACIs and RAs inhibit neuroblastoma in significantly lower concentrations when used together than when used individually. Combination therapy may improve the ultimate efficacy while reducing the side effects of these agents in clinical use.

L3 ANSWER 29 OF 44 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:478614 BIOSIS
DOCUMENT NUMBER: PREV200510270518
TITLE: Histone deacetylase inhibitors and filgrastim do not synergize with ATRA in the induction of changes of acute promyelocytic leukemia cells adhesive properties.
AUTHOR(S): De Santis, Gil C. [Reprint Author]; Moreno, Suzana E.; Teixera, Hamilton L. G.; Lima, Ana Silvia G; Garcia, Aglair B.; Falcao, Roberto P.; Cunha, Fernando Q.; Rego, Eduardo M.
CORPORATE SOURCE: Univ Sao Paulo, Med Sch Ribeirao Preto, Dept Internal Med, BR-05508 Sao Paulo, Brazil
SOURCE: Blood, (NOV 16 2004) Vol. 104, No. 11, Part 1, pp. 698A. Meeting Info.: 46th Annual Meeting of the American-Society-of-Hematology. San Diego, CA, USA. December 04 -07, 2004. Amer Soc Hematol. CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005

AB All-trans retinoic acid (ATRA) in combination with anthracyclines induces longterm complete remission in approximately 80% of patients with acute promyelocytic leukemia (APL). However, ATRA causes the retinoic acid syndrome (RAS) characterized by respiratory distress, pleural effusions, fever and weight gain. RAS is associated with changes in the expression of adhesion molecules (AMs) in the leukemic blasts. Nevertheless, which AMs are essential to RAS development is not clear. In addition, the effect on AMs expression of new therapeutic agents for APL such as historic deacetylase inhibitors (HDACis) or filgrastim is presently unknown. HDACis have been successfully used to treat ATRA-reftactory cases and they potentiate ATRA-induced

differentiation. The association of ATRA+ filgastrim induced remission in an APL patient harboring the t(I 1; 1 7)/PLZF/RAR alpha, which is resistant to ATRA. In order to determine the effect of ATRA, filgrastim, HDACis and their associations on cell adhesion, we analyzed the expression of the AMs: CD I I a, CD11b, CD 18, CD29, CD54 CD62L and CD162 on leukemic cells from 18 patients with APL and in NB4 cells treated ex vivo for 12 hours with DMSO (control), ATRA (I mM), filgrastrim (100ng/mL), trichostatin A (TSA, 0.1 mM), phenyl butirate (PB, I mM) (the latter two are bona fine HDACis), ATRA+TSA, ATRA+PB and ATRA+filgrastim (at the same doses). The number of positive cells for each of this markers and their respective fluorescence intensity was determined by flow cytometry. We detected a significant increase in the number of CD54(+) and CD18(+) cells, associated with an increase in the intensity of expression of CD54, CD I I a, CD11b and CD 18 in both NB4 and primary cells treated with ATRA alone or associated with PB or G-CSF. No difference was observed between samples treated exclusively with ATRA and those with the associations. We then analyzed if the changes in AMs expression were accompanied by changes in the adhesion to Matrigel or endothelial cells. ATRA and its associations, but not TSA, PB or filgrastim alone, increased significantly cell adhesion in vitro, an effect that was reversed by pre-incubating treated cells with anti-CD54 or anti-CD18 antibodies (Abs), or with dexametasone. ATRA induced cell adhesion was not dependent on myeloid maturation as it could be detected after short (12h) incubations. Finally, we analyzed the effects of ATRA, filgrastim and their association in a mouse model. NB4 cells were treated with ATRA, filgrastim, ATRA+filgrastim and injected IV through the tail vein. After 6h mice, the number of myeloid cells retained in the lungs was evaluated by measuring the myeloperoxidase activity. Compared tocontrol groups (untreated cells or saline), the ATRA and ATRA+filgrastim but not the Filgrastim alone group presented a significant increase in the number of myeloid cells infiltrating the lungs. Similarly to the observed in vitro, pre incubation with anti-CD54, anti-CD18 Abs or with dexametasone reversed the increased cell adhesion in vivo. In conclusion, our results show that treatment with HDACis or filgrastim alone do not affect AM expression or cell adhesionand that there is no significant synergism between these agents and ATRA. In addition, our data suggest that SAR development is dependent on ATRA induced changes in CD54 and CD18 expression.

L3 ANSWER 30 OF 44 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:477875 BIOSIS
DOCUMENT NUMBER: PREV200510269779
TITLE: Phase 2 trial of the histone deacetylase inhibitor valproic acid as a monotherapy or in combination with all-trans retinoic acid in 24 patients with acute myeloid leukemia.
AUTHOR(S): Kuendgen, Andrea [Reprint Author]; Strupp, Corinna; Hildebrandt, Barbara; Knipp, Sabine; Junge, Baerbel; Haas, Rainer; Germing, Ulrich; Gattermann, Norbert
CORPORATE SOURCE: Univ Dusseldorf, D-4000 Dusseldorf, Germany
SOURCE: Blood, (NOV 16 2004) Vol. 104, No. 11, Part 1, pp. 501A. Meeting Info.: 46th Annual Meeting of the American-Society-of-Hematology. San Diego, CA, USA. December 04 -07, 2004. Amer Soc Hematol. CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005

AB Valproic acid (VPA) has been shown to inhibit historic deacetylase activity, and to synergize with ATRA in the differentiation

induction of leukemic myeloidblast cells in vitro. We applied VPA to 20 patients (16 sAML/ MDS, 2 de-novo-AML, 2 sAML/OMF) too old or physically unfit to receive intensive chemotherapy. VPA monotherapy was targeted to reach serum concentrations of 50-100mg/ml. ATRA was added (80mg/m2/d in two divided doses, every other week) in some of the patients who did not respond or who relapsed. To enhance responses, we treated an additional 4 patients (2 sAML/MDS, 1 sAML/ET, I de novo AML) with VPA+ATRA from the start. Median age was 70 years (51-84). Median bone marrow blast count was 30% (10-80). 5 patients had only 10-15% marrow blasts but were included because they showed treatment failure or relapse after chemotherapy and were unable to receive further cytotoxic treatment. Median treatment duration was99 days (20396) for VPA and 79 days (18-339) for ATRA. Responses according tointernational working group (IWG, Cheson et al., 2003) criteria were observedin 5 patients (25%) on VPA monotherapy (4PR, 1CR). Of the responding patientstwo have ongoing responses (CR, PR) for 12 and 13 months, respectively. I patient reaching PR discontinued VPA when her physical condition had improved sufficiently to allow further chemotherapy. I patient relapsed after 2 months andwas switched to VPA+ATRA, without response. I patient died of infectious complications. 8 additional patients showed stable disease without increases in peripheral blast count. Responses lasted for a median of 4 months (2-13). Among the 4 patients receiving VPA+ATRA from the start, 1 (25%) achieved PR. When hestopped VPA after 3 months because of side effects, he continued oil ATRA, achieving a CRi (CR with incomplete recovery of platelets) lasting for 8 months.4 of 14 nonresponders were switched to VPA+ATRA, but none of them showed a response. Response to VPA treatment was not associated with FAB subtype or karyotype. Median bone marrow blast count was 28 (13-45)% in responders, 30 (10-75)% in patients with stable and 41 (25-80)% in patients with progressive disease. Since our patients mainly had secondary AML, we also analyzed our results according to the proposals of the IWG for MDS (Cheson et al., 2000). Among patients receiving VPA monotherapy I patient had a major trilineage response. 2 patients showed a minor erythroid and one a minor neutrophil response. In the second group of patients one had a major erythroid response. Concerning side effects, VPA caused tremor in four cases, leading to cessation of treatment in two. Regarding ATRA, grade 1-2 skin toxicity was observed in 4, grade 1-2 gastrointestinal toxicity in 2, and pleural effusion in I patient. In summary, we observed responses according to IWG criteria in 25% of our patients (6/24). The best responses to VPA or VPA+ATRA in AML patients occurred in patients with lowblast count, mainly in patients who showed relapsed or refractory disease shortly after intensive chemotherapy. These data indicate that VPA might be most effectively applied after or in addition to intensive chemotherapy.

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ACCESSION NUMBER: 2004:197750 BIOSIS
DOCUMENT NUMBER: PREV200400198309
TITLE: beta - Catenin and RA synergistically induce ES cells into the neuronal lineage.
AUTHOR(S): Otero, J. J. [Reprint Author]; Kessler, J. A. [Reprint Author]
CORPORATE SOURCE: Neurol., Northwestern Univ, Chicago, IL, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 347.2. http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English

ENTRY DATE: Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004

AB Neural differentiation of embryonic stem (ES) cells is inhibited by culture at high density. This inhibition requires cell-cell/matrix interactions but is not reproduced by activating notch signaling at low densities. Although neuronal differentiation of ES cells cultured at low density is promoted by retinoic acid (RA) treatment, culture of ES cells at higher density inhibits RA-mediated differentiation. By contrast, overexpression of beta-catenin or stabilization of beta-catenin by treatment with Wnt 3a conditioned medium promotes neurogenesis in high density cultures even in the absence of RA. However, RA treatment potentiates the effects of beta-catenin signaling in high density culture. The majority of the neurons made from ES cells by RA treatment, beta-catenin overexpression, or both were found to be gabaergic. We attempted to look at this synergistic interplay between RA and beta-catenin signaling by examining pitx2 expression. Pitx2 is a bicoid related homeobox transcription factor that is involved in gabaergic neuron formation. Previous reports have shown pitx2 to be downstream of the Wnt/beta-catenin signaling pathway and the RA signaling pathway. RA treatment was found to upregulate pitx2 expression in low density cultures where beta-catenin is in a more active state, but not in high density cultures where beta-catenin signaling is less active. Interestingly, cells overexpressing beta-catenin were found to upregulate pitx2 when cultured at high density whereas control cells did not. Furthermore, stimulation of this pathway by treatment with the histone deacetylase inhibitor Trichostatin-A resulted in increased neuronal differentation. In this study we examine the role of pitx2 in neuronal differentiation and determination of neuronal subtype identity in murine ES cells.

L3 ANSWER 32 OF 44 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:155085 BIOSIS
DOCUMENT NUMBER: PREV200400148524
TITLE: Upregulation of MDR1 and induction of doxorubicin resistance by synergistic use of histone deacetylase inhibitor depsipeptide (FK228) and ATRA in acute promyelocytic leukemia cells.
AUTHOR(S): Tabe, Yoko [Reprint Author]; Konopleva, Marina [Reprint Author]; Contractor, Rooha [Reprint Author]; Igari, Jun; Andreeff, Michael [Reprint Author]
CORPORATE SOURCE: Blood and Marrow Transplantation, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 860a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB The MDR1 gene product, P-glycoprotein (P-gp), functions as a transmembrane efflux pump for a variety of chemotherapeutic drugs including anthracyclines. Acute promyelocytic leukemia (APL) cells lack MDR1 expression and are characterized by high sensitivity to anthracyclines. Recently, MDR1 gene expression was reported to be silenced by epigenetic mechanisms involving histone deacetylases (HDAC) and DNA methyltransferases. APL is associated with an oncogenic transcription

factor PML-RARa that represses the RA receptor target gene transcription through histone deacetylation. The PML-RARa chimeric protein, moreover, has been suspected as the factor suppressing MDR1 through chromatin remodeling. In this study, we investigated the combined effects of ATRA and the novel HDAC inhibitor depsipeptide (FK228) on MDR1 mRNA expression in NB4 APL cells by TaqMan RT-PCR. ATRA alone (1muM) induced MDR-1 mRNA (10-fold), and FK228 induced MDR1 in a dose-dependent fashion (3nM 17fold, 5nM 45fold), compared with controls. The ATRA/FK228 (3nM) combination enhanced MDR1 mRNA expression 45fold, compared with controls. We then investigated ATRA (1muM)/FK228(3nM) effects on doxorubicin (DOX)-induced cytotoxicity. Pre-treatment with ATRA or FK228 alone did not affect DOX-induced apoptosis (annexin V positivity control 25%; ATRA 27%; FK228 21%; DOX 55%; ATRA followed by DOX 55%, FK228 followed by DOX 62%). However, prior exposure to ATRA/FK228 slightly reduced DOX induced-apoptosis in NB4 cells (ATRA/FK228 22%; DOX 55%; ATRA/FK228 followed by DOX 43%). In contrast, ATRA/FK228 treatment following DOX enhanced induction of apoptosis (control 27%; ATRA 20%; FK228 15%; ATRA/FK228 16%; DOX 50%; DOX followed by ATRA 57%, followed by FK228 69%, followed by ATRA/FK228 79%; $p<0.05$ compared with ATRA/FK228 followed by DOX). Another HDAC inhibitor suberoylanikide hydroxamic acid (SAHA) combined with ATRA similarly affected sensitivity of APL cells to doxorubicin. Experiments aimed at the identification of the critical histone residue modified by ATRA and/or FK228 on the MDR1 promoter using quantitative chromatin immunoprecipitation (ChIP) by TaqMan PCR are ongoing. As doxorubicin induces apoptosis of cells in the G2 phase, we investigated potential cell cycle effects of FK228 and ATRA/FK228. FK228 at 3nM induced G1 arrest and ATRA/FK228 enhanced this arrest (% cells in G1: control 43%, ATRA 64%, FK228 57%, ATRA/FK228 79%; $p<0.01$ compared with ATRA). In conclusion, we here demonstrate for the first time that ATRA/HDAC inhibitor combinations increase MDR1 mRNA expression in APL that mediates resistance to doxorubicin-induced apoptosis. Furthermore, the cell cycle data indicate that induction of G1 arrest by ATRA/HDAC inhibitors may contribute to doxorubicin resistance. DOX followed by the ATRA/HDAC inhibitor combination was therefore much more cytotoxic than the same drugs given in reverse sequence. These studies establish the criticality of biologically correct sequential therapy in future clinical trials with combinations of HDAC inhibitors, ATRA and anthracyclines.

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ACCESSION NUMBER: 2004:155080 BIOSIS
DOCUMENT NUMBER: PREV200400148519
TITLE: Dithiophenes potentiate differentiation of APL cells by lowering the threshold for ligand mediated co-repressor/co-activator exchange with RARalpha and enhancing changes in ATRA regulated gene expression.
AUTHOR(S): Xu, Ke [Reprint Author]; Chung, Danna [Reprint Author]; Glasow, Annegret [Reprint Author]; Jing, Yongkui; Guidez, Fabien [Reprint Author]; Stegmaier, Kimberly; Golub, Todd R.; Zelent, Arthur [Reprint Author]; Waxman, Samuel
CORPORATE SOURCE: Leukemia Research Fund Center, Institute of Cancer Research, London, UK
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 859a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English

ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB Combinatorial use of agents with synergistic anti-leukemic activities has emerged as an effective strategy for reducing single agent toxicities and enhancing the overall therapeutic effects. A number of such combinatorial approaches have been explored in differentiation therapy of acute promyelocytic leukemia (APL), using retinoid and non-retinoid agents such as arsenic compounds or histone deacetylase (HDAC) inhibitors, for example. In a cell-differentiation based screen of 400 compounds, dithiophenes were found to specifically potentiate differentiation induction of APL cells by all-trans-retinoic acid (ATRA) (Waxman, S. et al., Blood 94:61A, 1999). In contrast to other agents, however, these effects required very low (nM) concentrations of the most potent dithiophene derivatives and were not associated with changes in global histone acetylation or methylation. Nevertheless, as observed for HDAC inhibitors, the action of dithiophenes on cell differentiation was reflected by their abilities to potentiate ATRA-mediated activation of PML-RARalpha as well as of the wild type RARalpha protein. Limited microarray analysts of gene expression indicated that the effects of ditniophenes on cell differentiation and activities of the RARalpha proteins were paralleled by enhancement of some but not all ATRA-modulated gene expression, possibly reflecting distinct mechanisms for dithiophene-sensitive and -insensitive ATRA regulation. Consistent with this hypothesis, genes whose ATRA-modulated expression was sensitive to dithiophenes possess regions of strong DNA sequence homology in their regulatory domains. Interestingly, both the positive and negative effects of ATRA on expression of specific genes were potentiated by dithiophenes. These genes could be classified into different functional categories, including transcription factors, cell cycle regulators and growth factors. Although low levels of dithiophenes alone had no effect on gene expression, when used at higher concentrations these compounds were able to inhibit NFkappaB activation, possibly reflecting their pro-apoptotic activities at muM levels against various tumor cell types. Investigating the mechanism underlying the effects of these drugs on ATRA-induced APL cell differentiation, we have shown that dithiophenes enhance ATRA-mediated dissociation and association of co-repressor N-CoR and co-activator p300 histone acetyltransferase, respectively, with the RARalpha proteins, and increase rate of PML-RARalpha protein degradation. These data suggest that dithiophenes act at a level of receptor activation, possibly by affecting posttranslational modification of the receptor, which leads to a decrease and increase in binding affinity of the receptor for co-repressor and co-activator, respectively. Given the specificities of these low dithiophene concentrations for PML-RARalpha and RARalpha, they may be useful drugs for combinatorial differentiation therapy of APL and possibly other AML subtypes.

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ACCESSION NUMBER: 2004:151955 BIOSIS
DOCUMENT NUMBER: PREV200400147610
TITLE: Effect of the histone deacetylase inhibitor valproic acid alone and in combination with all-trans retinoic acid on t(15;17) positive leukemic cells.
AUTHOR(S): Drescher, Bettina [Reprint Author]; Goerlich, Kerstin [Reprint Author]; Doehring, Axel [Reprint Author]; Ganser, Arnold [Reprint Author]; Heil, Gerhard [Reprint Author]; Krauter, Juergen [Reprint Author]
CORPORATE SOURCE: Department Hematology and Oncology, Hannover Medical School, Hannover, Germany
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 620a.

print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB The translocation t(15;17)(q22;q21) is the genetic hallmark of acute promyelocytic leukemia fusing the PML gene to the retinoic acid receptoralpha (RARalpha) gene thus resulting in the PML/RARalpha fusion protein: PML/RARalpha recruits histone deacetylases as well as methyl transferases and represses target genes of wild-type RARalpha resulting in a block of myeloid differentiation. It has been shown that all-trans retinoic acid (ATRA), arsenic trioxide and histone deacetylase inhibitors like trichostatin A and sodium buryrate can overcome these effects and induce differentiation and apoptosis in PML/RARalpha positive cells. Recently, the anticonvulsant drug valproic acid (VPA) has been described as a novel histone deacetylase inhibitor. We therefore examined the effect of VPA on the t(15;17) positive cell line NB4 comparing it to ATRA-mediated differentiation. Moreover, the effect of VPA on the ATRA-resistant NB4-R2 cell line was analysed. Incubation of NB4 cells with VPA led to a concentration-dependent increase of acetylated histone H4 in western blot analysis of nuclear extracts. Incubation with ATRA had no effect on histone acetylation. NB4 cells treated with ATRA displayed a substantial upregulation of CD11b and CD11c surface expression. Real time RT-PCR revealed an increased expression of the myeloid transcription factors C/EBPbeta and C/EBPepsilon and a downregulation of c-myc mRNA. VPA also led to CD11b and CD11c surface expression as well as c-myc downregulation whereas it had no effect on C/EBPbeta and C/EBPepsilon. VPA and ATRA were synergistic with regard to CD11b and CD11c upregulation and c-myc downregulation. In NB4-R2 cells, the effect of ATRA on the expression of CD11b and CD11c as well as on C/EBPbeta, C/EBPepsilon and c-myc mRNA was markedly reduced in comparison to the parental NB4 line. In contrast, the effect of VPA was identical in both cell lines. A synergistic effect of ATRA and VPA on CD11b and CD11c expression was also present in the NB4-R2 cells. Taken together, VPA acts as an inhibitor of histone deacetylases in t(15;17) positive cells and induces myeloid differentiation. In contrast to ATRA, VPA does not induce C/EBPbeta and C/EBPepsilon as target genes while both substances result in a downregulation of c-myc. The effect of VPA on t(15;17) positive cells is not affected by ATRA-resistance. Therefore, in the future this substance might be helpful in patients with ATRA-resistant disease.

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ACCESSION NUMBER: 2004:150184 BIOSIS
DOCUMENT NUMBER: PREV200400146876
TITLE: Valproic acid alone or in combination with all-trans-retinoic acid (ATRA) for the treatment of myelodysplastic syndromes and sAML/MDS.
AUTHOR(S): Kuendgen, Andrea M. [Reprint Author]; Strupp, Corinna [Reprint Author]; Tapprich, Christoph [Reprint Author]; Hildebrandt, Barbara; Habersang, Kerstin [Reprint Author]; Junge, Baerbel [Reprint Author]; Aivado, Manuel [Reprint Author]; Haas, Rainer [Reprint Author]; Germing, Ulrich [Reprint Author]; Gattermann, Norbert [Reprint Author]

CORPORATE SOURCE: Hematology, Oncology, and Clinical Immunology, Heinrich-Heine-University, Duesseldorf, Germany
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 428a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB Histone acetylation plays an important role in the regulation of gene transcription. Valproic acid (VPA), a widely used anticonvulsant drug, has recently been shown to inhibit histone deacetylase (HDAC) activity at concentrations within the therapeutic range for treatment of seizures, and to synergize with ATRA in the differentiation induction of AML blasts in vitro. Since myelodysplastic syndromes are characterized by unpaired maturation, differentiation induction is an attractive therapeutic approach. We treated 20 patients with either VPA monotherapy (n=15) (7 RA, 2 RARS, 2 RAEB I, 2 RAEB II, 1 CMML, 1 sAML/MDS), or with a combination of VPA+ATRA (n=5) (2 RA, 1 RAEB i, 2 sAML/MDS). VPA was administered to reach a serum concentration between 50 and 10mug/ml. ATRA was given at a dose of 80mg/m2/d in two divided doses, every second week. To be evaluable, patients had to be treated for at least 8 weeks. All patients gave written informed consent. Hematological improvement, according to international working group (IWG) criteria, was observed in 6 patients on VPA monotherapy: 2 major platelet, 1 major erythroid, 1 minor erythroid, and 1 major neutrophil response, as well as 1 PR with trilineage response. One patient with RAEB II had a peripheral blast clearance and a reduction of bone marrow blasts (16% to 10%) in addition to his major platelet response. Another patient (RAEB II) showed an increase in platelet count from 33.000/mul to 138.000/mul. This response was not sufficient to fulfill IWG criteria because of a duration of only 36 days, due to AML transformation. Of the responding patients, five relapsed after a median of 104 days. 4/5 patients relapsing after VPA were switched to the combination; two of them responded again, both for more than 9 months now. Of the 8 patients who never responded to VPA, 4 were switched to the combined treatment, but without success. In patients receiving VPA+ATRA from the start, there was no response according to IWG criteria. However, one patient with sAML/MDS showed a peripheral blast clearance (down from 27%) and a reduction of bone marrow blasts (from 45% to 10%). After VPA Was discontinued because of vertigo, he had a major platelet response, as well as a blast clearance and complete cytogenetic response in the bone marrow. Response to VPA treatment was not associated with either WHO subtype, IPSS risk group or karyotype. Side effects were generally mild. Only one patient discontinued VPA because of vertigo and tremor. Thrombocytopenia occurred in 5 patients, especially in the combination group, but was associated with disease progression in at least 2 patients. In the others, the decrease in platelet counts was reversed after cessation of VPA. We conclude that valproic acid is a well tolerated oral treatment with significant effects in MDS. However, we have the impression that VPA monotherapy is not sufficiently active to achieve prolonged benefits. Rather, valproic acid looks like a promising new candidate for combination regimens.

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ACCESSION NUMBER: 2003:368080 BIOSIS

DOCUMENT NUMBER: PREV200300368080
TITLE: Preliminary Experience with Valproic Acid in Association to Differentiative Agents and Low Dose Chemotherapy in Poor Prognosis AML.
AUTHOR(S): Ferrero, Dario [Reprint Author]; Campa, Elisabetta [Reprint Author]; Campana, Silvia [Reprint Author]; Dellacasa, Chiara [Reprint Author]; Boccadoro, Mario [Reprint Author]
CORPORATE SOURCE: Divisione di Ematologia, Universita degli Studi di Torino, Torino, Italy
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 4596. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003
AB In our previous experience, the combination of in vitro active differentiation inducers (13-cis retinoic acid + 1;25(OH)2vitamin D3) + low dose 6-thioguanine has determined hematological improvements in about 50% of poor prognosis myelodysplastic syndrome patients (Ferrero D et al.: Leuk Res 1996; 20: 867-876; Blood 1999; 10 suppl.1,abstract 1372). The same combination + low dose ARA-C has been employed in AML patients unsuitable to intensive treatments with encouraging results (manuscript in preparation). Valproic acid, a widely employed anticonvulsant drug, has been recently proved to inhibit , at therapeutical concentrations, histone-deacetylase (Phiel CJ et al.; J Biol Chem 2001; 276: 36734-36741), an enzyme regarded as a key mediator of differentiation block in AML (Minucci S et al.: Oncogene 2001; 20: 3110-3115). Indeed, valproic acid has been demonstrated to synergize in vitro with retinoids to induce AML cell differentiation (Ferrara F et al.: Cancer Res 2001; 61: 2-7). We recently started a clinical experience by combining low-dose valproic acid (200-600 mg/day) to differentiating agents and low dose chemotherapy in poor prognosis AML patients unsuitable to intensive treatments, after informed consent was obtained. One patient (81 year old) was in myeloid blastic phase of chronic myeloid leukemia (CML) and had not received previous differentiative therapy. Since he could not be enrolled in protocols with STI571, he was treated with valproic acid (200 mg/day) combined to 13-cis retinoic acid (20 mg/day), dihydroxylated vitamin D3 (1ug/day) and low dose (40 mg/day), intermittent 6-thioguanine. Seven more patients (median age 67, 52-81) had AML (1 M1, 3 M2, 1 M4, 2 RAEB-t of previous F.A.B. classification of MDS), that, in four patients, was secondary to previous MDS. All 7 patients had been unresponsive to or had relapsed after low dose ARA-C + 6-thioguanine + 13-cis retinoic acid and dihydroxylated vitamin D3. They have been retreated with the same combination of ARA-C (8mg/m2 x 2/day for 14 days) alternated to 6-thioguanine (40 mg/day for 21 days) + dihydroxylated vitamin D3 (1ug/day), with the addition of valproic acid (400-600 mg/day) and with all-trans retinoic acid (ATRA)(30 mg/m2/day for 14 days every 3 weeks) substituting for 13-cis retinoic acid. Therapy was well tolerated with the exception of 2 AML patients: one complained of confusion and lethargy with 600 mg valproic acid, symptoms regressed by lowering the dosage but the patient refused further treatment; another patient was intolerant to ATRA (headpain and vomiting) and went back to 13-cis retinoic acid treatment. The patient with blastic phase CML returned to chronic phase with less than 5% BM blasts and no more transfusion requirement: the response lasted for more than 10 months until the patient died of second cancer. Among the 6 evaluable AML patients, we

observed a 6 month 2nd complete remission, a minor response and two stable disease lasting 8+, 2+ and 4 months, respectively. Two patients did not respond and died in one month, the others are alive 2-9 months from the start of therapy. Our preliminary results suggest that the addition of well tolerated doses of valproic acid to retinoids + low dose chemotherapy may enhance the responsiveness to differentiative treatments. Such a combination is worthy to be tested as a front-line therapy for AML patients unsuitable to aggressive chemotherapy.

L3 ANSWER 37 OF 44 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:305376 BIOSIS
DOCUMENT NUMBER: PREV200100305376
TITLE: A phase IIb trial of all-trans retinoic acid (ATRA) combined with bryostatin 1 (BRYO) in patients (pts) with myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML).
AUTHOR(S): Stone, Richard [Reprint author]; DeAngelo, Daniel [Reprint author]; Galinsky, Ilene [Reprint author]; Yang, Xinping [Reprint author]; Daftary, Farah [Reprint author]; Xu, Guangin [Reprint author]; Liou, Simon [Reprint author]
CORPORATE SOURCE: Dana-Farber Cancer Institute, Boston, MA, USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 265b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

AB ATRA, a vitamin A derivative, and BRYO, a macrocyclic lactone isolated from the marine organism B. neritina, synergistically induce monocytic differentiation in human AML cell lines via up-regulation and activation of protein kinase Cbeta (PKCbeta) which initiates cell signaling cascades. A trial in solid tumor pts determined the maximally tolerated dose (MTD) of BRYO that could be given with ATRA at its MTD. We performed a randomized phase IIb trial in which pts with MDS or AML (relapsed/refractory and/or not a chemotherapy candidate) were given ATRA (75 mg/m2 po bid on d1-8, 15-22) in combination with BRYO (60 ug/m2 over 30 min or 40 ug/m2/d for 72 h on d 8 and 22). 40 pts (27M/13F; age 38-80; median 68 years) were enrolled (17 with MDS (RAEB/RAEB-T (9); RA/RARS (8)) and 23 with AML (relapsed/refractory (12); initial treatment (rx) in pts > age 60 years (11))). 38 are evaluable (eval) for toxicity (2 dropped out before BRYO due to sepsis (1) and rapid disease progression (1)) and 36 for response (4 dropped out between d 8-28 due to sepsis, disease progression, or other). While disease-related Gr 3/4 sepsis (9) and GI toxicities (5) were noted, serious study drug-related toxicites were limited to cardiac ischemia (1), severe bone pain (1), and BRYO 30 min infusion-related facial flushing and shortness of breath (4) which did not recur upon rechallenge in 3. Although there were no complete or partial remissions, 9 (25% of eval pts, 5 in the BRYO 30 min arm) experienced a sustained improvement by at least 50% in at least one parameter; 8 had a reduction in bone marrow blasts and 5 had an improvement in a cytopenia. 8 pts received at least one additional 22 d cycle. The PKCbeta protein level in ficoll-isolated blood mononuclear cells (MNCs), measured by Western blotting of cytoplasmic extracts compared to an actin control, was down-regulated in the cytoplasm (which correlates with enzyme activation) after 15-45 min relative to the start of BRYO rx in 11/11 pts who received BRYO over 30 min and after 1-3d in 7/11 courses in 7 pts who received the

72 h infusion. These results demonstrate that ATRA in combination with BRYO (at both 30 min and 72 h infusion duration) is well tolerated in pts with MDS and AML, has the predicted effect on PKCbeta levels and posesses some clinical activity. Future trials of this combination plus other differentiation inducers, including histone deacetylase or DNA methylation inhibitors, may be warranted.

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ACCESSION NUMBER: 2001:301455 BIOSIS
DOCUMENT NUMBER: PREV200100301455
TITLE: Multiple mechanisms are involved in differentiation induced by arsenic trioxide in acute promyelocytic leukemia.
AUTHOR(S): Shen, Y. L. [Reprint author]; Zhu, Q. [Reprint author]; Cai, X. [Reprint author]; Yu, Y. [Reprint author]; Jia, P. M. [Reprint author]; Chen, G. Q. [Reprint author]; Wang, Z. Y. [Reprint author]; Chen, S. J. [Reprint author]; Chen, Z. [Reprint author]
CORPORATE SOURCE: Shanghai Institute of Hematology, Rui Jin Hospital, Shanghai Second Medical University, Shanghai, China
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 310a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

AB The dramatic clinical remission following arsenic trioxide (As2O3) treatment of most acute promyelocytic leukemia (APL) patients, even those in relapse after all-trans retinoic acid (RA) treatment has revived interest in this ancient traditional Chinese medicine. In vitro As2O3 exerts dose-dependent dual effects in the APL cell line NB4: high dose (1.0apprx2.0muM) triggers apoptosis, while low dose (0.1apprx0.5muM) induces partial differentiation. Though progress has been made in understanding the mode of action of As2O3-induced apoptosis, the mechanism of low dose As2O3-induced differentiation remains obscure. In this work we tried to elucidate the mechanism of low dose As2O3-induced APL cell differentiation. Our preliminary data show that low dose (0.25muM) As2O3 causes hyperacetylation of histone H3 and H4, induces the expression of some RA-induced genes and slightly stimulates RARE-luciferase reporter activities, although As2O3 could not dissociate SMRT from PML-RARalpha or RARalpha under isolated in vitro conditions. BMS614, a RARalpha specific antagonist, has no effect on As2O3-induced partial differentiation suggesting that As2O3-induced differentiation is not mediated directly by the RARalpha signaling pathway, and another underlying mechanism such as inhibition of histone deacetylase may play a major role. On the other hand, the restoration of NB4 cell sensitivity to physiological concentration of RA following PML-RARalpha degradation by low dose As2O3, and the synergistic differentiation induced by low dose As2O3 and RA identifies another mechanism. Recently it was reported that histone deacetylase inhibitors synergize with RA to induce differentiation of a RA-resistant APL cell line. We tested the effect of trichostatin A (TSA) on RA sensitive NB4 cells and RA-resistant MR2 cells. We find that low dose (20ng/ml) TSA enhances the differentiation of APL cells treated with As2O3 or RA and partially restores the responsiveness of RA-resistant MR2 cells to RA and As2O3. Taken together, As2O3-induced differentiation may result from a

combination of several effects, some of which occur in a non-ligand dependent manner.

L3 ANSWER 39 OF 44 EMBASE

ACCESSION NUMBER: 2004489465 EMBASE
TITLE: The epigenetics of ovarian cancer drug resistance and resensitization.
AUTHOR: Balch, Curtis; Nephew, Kenneth P.
CORPORATE SOURCE: Medical Sciences, Indiana University, Bloomington, Ind. knephew@indiana.edu
AUTHOR: Huang, Tim H.-M.
CORPORATE SOURCE: Department of Molecular Virology, Immunology and Medical Genetics, Compreh. Cancer Ctr., Ohio State U..
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SOURCE: American Journal of Obstetrics and Gynecology, (Nov 2004) Vol. 191, No. 5, pp. 1552-1572.
Refs: 260
ISSN: 0002-9378 CODEN: AJOGAH
PUBLISHER IDENT.: S 0002-9378(04)00508-3
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
022 Human Genetics
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Dec 2004
Last Updated on STN: 2 Dec 2004

AB Ovarian cancer is the most lethal of all gynecologic neoplasms. Early-stage malignancy is frequently asymptomatic and difficult to detect and thus, by the time of diagnosis, most women have advanced disease. Most of these patients, although initially responsive, eventually develop and succumb to drug-resistant metastases. The success of typical postsurgical regimens, usually a platinum/taxane combination, is limited by primary tumors being intrinsically refractory to treatment and initially responsive tumors becoming refractory to treatment, due to the emergence of drug-resistant tumor cells. This review highlights a prominent role for epigenetics, particularly aberrant DNA methylation and histone acetylation, in both intrinsic and acquired drug-resistance genetic pathways in ovarian cancer. Administration of therapies that reverse epigenetic "silencing" of tumor suppressors and other genes involved in drug response cascades could prove useful in the management of drug-resistant ovarian cancer patients. In this review, we summarize recent advances in the use of methyltransferase and histone deacetylase inhibitors and possible synergistic combinations of these to achieve maximal tumor suppressor gene re-expression. Moreover, when used in combination with conventional chemotherapeutic agents, epigenetic-based therapies may provide a means to resensitize ovarian tumors to the proven cytotoxic activities of conventional chemotherapeutics. .COPYRGT. 2004 Elsevier Inc. All rights reserved.

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ACCESSION NUMBER: 2004318012 EMBASE
TITLE: Accelerated and blastic phases of chronic myelogenous leukemia.
AUTHOR: Giles, Francis J., Dr. (correspondence); Cortes, Jorge E.; Kantarjian, Hagop M.; O'Brien, Susan M.
CORPORATE SOURCE: Department of Leukemia, The University of Texas, M.D. Anderson Cancer Ctr., 1515 H., Houston, TX, United States. fgiles@mdanderson.org
SOURCE: Hematology/Oncology Clinics of North America, (Jun 2004) Vol. 18, No. 3, pp. 753-774.
Refs: 177
ISSN: 0889-8588 CODEN: HCNAEQ
PUBLISHER IDENT.: S 0889-8588(04)00010-3
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Aug 2004
Last Updated on STN: 12 Aug 2004

AB Although the mechanisms of CML transformation remain poorly understood, recent therapeutic advances moderately have improved the prognosis of patients in AP and BP. Treatment with IFN-αbased regimens are minimally effective for patients in AP and ineffective for those in BP. Imatinib mesylate has a significant but generally transient response rate in patients in AP and BP. Hope for progress in this area lies mainly in the development of novel targeted therapies. The more promising agents that are being investigated include decitabine, HHT, troxacitabine, clofarabine, farnesyl transferase inhibitors, histone deacetylase inhibitors, and the VEGF and mTOR inhibitors. Many of these approaches may be synergistic with imatinib or the more powerful abl or Src inhibitors that are in development.

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ACCESSION NUMBER: 2004309977 EMBASE
TITLE: Enhancement by other compounds of the anti-cancer activity of vitamin D3 and its analogs.
AUTHOR: Studzinski, George P.
CORPORATE SOURCE: Pathol. Lab. Med. UMD-New Jersey M., 185 South Orange Avenue, Newark, NJ 07103-2824. studzins@umdnj.edu
AUTHOR: Danilenko, Michael
SOURCE: Experimental Cell Research, (15 Aug 2004) Vol. 298, No. 2, pp. 339-358.
Refs: 280
ISSN: 0014-4827 CODEN: ECREAL
PUBLISHER IDENT.: S 0014-4827(04)00249-6
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Aug 2004

Last Updated on STN: 5 Aug 2004

AB Differentiation therapy holds promise as an alternative to cytotoxic drug therapy of cancer. Among compounds under scrutiny for this purpose is the physiologically active form of vitamin D3, 1,25-dihydroxyvitamin D3, and its chemically modified derivatives. However, the propensity of vitamin D3 and its analogs to increase the levels of serum calcium has so far precluded their use in cancer patients except for limited clinical trials. This article summarizes the range of compounds that have been shown to increase the differentiation-inducing and antiproliferative activities of vitamin D3 and its analogs, and discusses the possible mechanistic basis for this synergy in several selected combinations. The agents discussed include those that have differentiation-inducing activity of their own that is increased by combination with vitamin D3 or analogs, such as retinoids or transforming growth factor-β and plant-derived compounds and antioxidants, such as curcumin and carnosic acid. Among other compounds discussed here are dexamethasone, nonsteroidal anti-inflammatory drugs, and inhibitors of cytochrome P450 enzymes, for example, ketoconazole. Thus, recent data illustrate that there are extensive, but largely unexplored, opportunities to develop combinatorial, differentiation-based approaches to chemoprevention and chemotherapy of human cancer.

L3 ANSWER 42 OF 44 EMBASE

ACCESSION NUMBER: 2003463397 EMBASE
TITLE: Fenretinide: A prototype cancer prevention drug.
AUTHOR: Malone, Winfred; Perloff, Marjorie; Crowell, James (correspondence)
CORPORATE SOURCE: National Cancer Institute, Division of Cancer Prevention, Chemoprev. Agent Devmt. Res. Group, Bethesda, MD, United States.
AUTHOR: Sigman, Caroline; Higley, Howard
CORPORATE SOURCE: CCS Associaties, 2005 Landings Drive, Mountain View, CA 94043, United States.
SOURCE: Expert Opinion on Investigational Drugs, (Nov 2003) Vol. 12, No. 11, pp. 1829-1842.
Refs: 150
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Dec 2003
Last Updated on STN: 1 Dec 2003

AB Fenretinide (N-4-hydroxyphenylretinamide [4-HPR]) is a synthetic retinoid that has been examined in in vitro assays, preclinical animal models and clinical trials as a cancer chemopreventive agent. Its pharmacology, toxicity and mechanisms of action initially suggested an increased therapeutic index relative to native retinolds for the control of tumours of the breast, prostate, bladder, colon, cervix and head and neck. Although fenretinide at the doses and schedules used in several pivotal Phase II and III clinical trials has not been proven to be efficacious in reducing the incidence of cancer or in retarding the development of preneoplastic lesions, encouraging observations regarding unanticipated preventative activity, such as for ovarian cancer control, have arisen from these studies. Research in cancer therapy and the elucidation of molecular pathways activated by fenretinide have also

yielded clues about how this agent might be better used in a prevention setting. Current trials are underway to re-examine both dose and schedule of fenretinide administration as well as the target tissues of interest. Investigations of potential synergism between fenretinide and other candidate chemopreventative molecules with complementary mechanisms of action may support future assessments of this prototype cancer prevention drug or its newer analogues.

L3 ANSWER 43 OF 44 EMBASE

ACCESSION NUMBER: 2003172219 EMBASE
TITLE: The interaction of histone deacetylase inhibitors and DNA methyltransferase inhibitors in the treatment of human cancer cells.
AUTHOR: Zhu, Wei-Guo (correspondence); Otterson, Gregory A.
CORPORATE SOURCE: Division of Hematology/Oncology, Department of Internal Medicine, The Ohio State University, 300 W, 10th Ave., Columbus, OH 43210, United States. otterson-1@medctr.osu.edu; zhu-1@medctr.osu.edu
AUTHOR: Zhu, Wei-Guo (correspondence)
CORPORATE SOURCE: The Ohio State University, Division of Hematology/Oncology, 1226 James Cancer Hospital, 300 W, 10th Ave., Columbus, OH 43210, United States. zhu-1@medctr.osu.edu
SOURCE: Current Medicinal Chemistry - Anti-Cancer Agents, (2003) Vol. 3, No. 3, pp. 187-199.
Refs: 178
ISSN: 1568-0118 CODEN: CMCACI
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 May 2003
Last Updated on STN: 19 May 2003
AB The potential anticancer activities of histone deacetylase (HDAC) inhibitors and DNA methyltransferase (DNMT) inhibitors have been extensively studied in recent years. HDAC inhibitors suppress the activities of multiple HDACs, leading to an increase in histone acetylation. This histone acetylation induces an enhancement of the expression of specific genes that elicit extensive cellular morphologic and metabolic changes, such as growth arrest, differentiation and apoptosis. DNMT inhibitors, such as 5-aza-cytidine (5-aza-CR) and 5-aza-2'-deoxycytidine (5-aza-CdR) are also widely studied because DNA hypomethylation induces the re-activation of tumor suppressor genes that are silenced by methylation-mediated mechanisms. Recently, the combination of HDAC inhibitors or demethylating agents with other chemo-therapeutics has gained increasing interest as a possible molecularly targeted therapeutic strategy. In particular, the combination of HDAC inhibitors with demethylating agents has become attractive since histones are connected to DNA by both physical and functional interactions. To date, the accumulating evidence has confirmed the hypothesis that the combination of HDAC and DNMT inhibition is very effective (and synergistic) in inducing apoptosis, differentiation and/or cell growth arrest in human lung, breast, thoracic, leukemia and colon cancer cell lines. This review will discuss the in vitro effects of HDAC inhibitors, such as trichostatin A (TSA), sodium butyrate, depsipeptide (FR901228, FK228), valproic acid (VPA) and suberoylanilide hydroxamic acid (SAHA), and the demethylating agent, 5-aza-CdR used alone and in combination treatment of human cancer cells

and the possible mechanisms involved.

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ACCESSION NUMBER: 2002293790 EMBASE
TITLE: Synergistic induction of mitochondrial damage and apoptosis in human leukemia cells by flavopiridol and the histone deacetylase inhibitor suberoylanilide hydroxamic acid (SAHA).
AUTHOR: Almenara, J.; Rosato, R.; Grant, S., Dr. (correspondence)
CORPORATE SOURCE: Division of Hematology/Oncology, Medical College of Virginia, Virginia Commonwealth University, MCV Station Box 230, Richmond, VA 23298, United States.
SOURCE: Leukemia, (2002) Vol. 16, No. 7, pp. 1331-1343.
Refs: 50
ISSN: 0887-6924 CODEN: LEUKED
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Sep 2002
Last Updated on STN: 5 Sep 2002

AB Interactions between the histone deacetylase inhibitor SAHA (suberoylanilide hydroxamic acid) and the cyclin-dependent kinase (CDK) inhibitor flavopiridol (FP) were examined in human leukemia cells. Simultaneous exposure (24 h) of myelomonocytic leukemia cells (U937) to SAHA (1 μM) and FP (100 nm), which were minimally toxic alone (1.5±0.5% and 16.3±0.5% apoptosis respectively), produced a dramatic increase in cell death (ie 63.2±1.9% apoptotic), reflected by morphology, procaspase-3 and -8 cleavage, Bid activation, diminished ΔΨm, and enhanced cytochrome c release. FP blocked SAHA-mediated up-regulation of p21CIP1 and CD11b expression, while inducing caspase-dependent Bc1-2 and pRb cleavage. Similar interactions were observed in HL-60 and Jurkat leukemia cells. Enhanced apoptosis in SAHA/FP-treated cells was accompanied by a marked reduction in clonogenic surivival. Ectopic expression of either dominant-negative caspase-8 (C8-DN) or CrmA partially attenuated SAHA/FP-mediated apoptosis (eg 45±1.5% and 38.2±2.0% apoptotic vs 78±1.5% in controls) and Bid cleavage. SAHA/FP induced-apoptosis was unaffected by the free radical scavenger L-N-acetyl cysteine or the PKC inhibitor GFX. Finally, ectopic Bcl-2 expression marginally attenuated SAHA/FP-related apoptosis/cytochrome c release, and failed to restore clonogenicity in cells exposed to these agents. Together, these findings indicate that SAHA and FP interact synergistically to induce mitochondrial damage and apoptosis in human leukemia cells, and suggest that this process may also involve engagement of the caspase-8-dependent apoptotic cascade.

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